
UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 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)

35 CambridgePark Drive, 4th Floor
Cambridge, Massachusetts
(Address of Principal Executive Offices)

45-3772460
(I.R.S. Employer
Identification No.)

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 October 31, 2021: 61,947,150

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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 tamibarotene, 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 pandemic 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 pandemic, additional or modified government actions, and the actions that may be required to contain the virus or treat its impact. The COVID-19 pandemic 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)

	September 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	\$ 115,420	\$ 173,984
Marketable securities	30,164	—
Accounts receivable	—	7
Contract assets	3,632	2,324
Prepaid expenses and other current assets	4,055	2,242
Total current assets	153,271	178,557
Property and equipment, net	13,458	14,213
Marketable securities - noncurrent	21,117	—
Other long-term assets	2,410	1,966
Restricted cash	3,086	3,086
Right-of-use asset – operating lease	14,299	14,831
Right-of-use assets – financing leases	402	597
Total assets	<u>\$ 208,043</u>	<u>\$ 213,250</u>
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	\$ 4,108	\$ 3,603
Accrued expenses	11,839	11,084
Deferred revenue, current portion	11,995	12,209
Financing lease obligations, current portion	285	265
Operating lease obligation, current portion	1,653	1,463
Total current liabilities	29,880	28,624
Deferred revenue, net of current portion	2,980	9,877
Financing lease obligations, net of current portion	140	356
Operating lease obligation, net of current portion	23,317	24,578
Warrant liability	5,594	19,711
Debt, net of debt discount, long term	40,072	39,551
Commitments and contingencies (See Note 9)		
Stockholders' equity:		
Preferred stock, \$0.001 par value; 10,000,000 shares authorized at September 30, 2021 and December 31, 2020; 0 shares issued and outstanding at September 30, 2021 and December 31, 2020	—	—
Common stock, \$0.001 par value; 200,000,000 shares authorized at September 30, 2021 and December 31, 2020; 61,942,950 and 56,222,746 shares issued and outstanding at September 30, 2021 and December 31, 2020, respectively	61	56
Additional paid-in capital	545,770	467,518
Accumulated other comprehensive loss	(5)	—
Accumulated deficit	(439,766)	(377,021)
Total stockholders' equity	106,060	90,553
Total liabilities and stockholders' equity	<u>\$ 208,043</u>	<u>\$ 213,250</u>

See accompanying notes to unaudited condensed consolidated financial statements.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Revenue	\$ 5,697	\$ 3,828	\$ 15,686	\$ 9,394
Operating expenses:				
Research and development	27,262	17,674	73,077	47,039
General and administrative	5,346	5,151	16,606	15,433
Total operating expenses	32,608	22,825	89,683	62,472
Loss from operations	(26,911)	(18,997)	(73,997)	(53,078)
Interest income	32	4	56	421
Interest expense	(984)	(493)	(2,921)	(1,251)
Change in fair value of warrant liability	1,836	—	14,117	—
Net loss applicable to common stockholders	\$ (26,027)	\$ (19,486)	\$ (62,745)	\$ (53,908)
Net loss per share applicable to common stockholders - basic and diluted	\$ (0.41)	\$ (0.43)	\$ (1.01)	\$ (1.19)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	62,928,299	45,781,638	62,394,819	45,137,331

See accompanying notes to unaudited condensed consolidated financial statements.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Net loss	\$ (26,027)	\$ (19,486)	\$ (62,745)	\$ (53,908)
Other comprehensive gain (loss):				
Unrealized holding gain (loss) on marketable securities	14	—	(5)	(24)
Comprehensive loss	<u>\$ (26,013)</u>	<u>\$ (19,486)</u>	<u>\$ (62,750)</u>	<u>\$ (53,932)</u>

See accompanying notes to unaudited condensed consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDER'S EQUITY
For the nine months ended September 30, 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	95,647	—	509	—	—	509
Vesting of restricted stock units	105,912	—	—	—	—	—
Issuance of shares under Employee Stock Purchase Plan	36,708	—	223	—	—	223
Stock-based compensation expense	—	—	7,909	—	—	7,909
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	—	—	—	(24)	—	(24)
Net loss	—	—	—	—	(53,908)	(53,908)
Balance at September 30, 2020	<u>45,807,878</u>	<u>\$ 45</u>	<u>\$ 392,786</u>	<u>\$ —</u>	<u>\$ (346,891)</u>	<u>\$ 45,940</u>
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	267,012	—	—	—	—	—
Issuance of shares under Employee Stock Purchase Plan	33,058	—	153	—	—	153
Stock-based compensation expense	—	—	7,479	—	—	7,479
Issuance of common stock in underwritten public offering, net of issuance costs of \$5,132	5,400,000	5	70,463	—	—	70,468
Other comprehensive loss	—	—	—	(5)	—	(5)
Net loss	—	—	—	—	(62,745)	(62,745)
Balance at September 30, 2021	<u>61,942,950</u>	<u>\$ 61</u>	<u>\$ 545,770</u>	<u>\$ (5)</u>	<u>\$ (439,766)</u>	<u>\$ 106,060</u>

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDER'S EQUITY
For the three months ended September 30, 2021
(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 June 30, 2020	45,758,881	\$ 45	\$ 389,766	\$ —	\$ (327,405)	\$ 62,406
Exercise of stock options	46,547	—	297	—	—	297
Vesting of restricted stock units	2,450	—	—	—	—	—
Stock-based compensation expense	—	—	2,723	—	—	2,723
Net loss	—	—	—	—	(19,486)	(19,486)
Balance at September 30, 2020	<u>45,807,878</u>	<u>\$ 45</u>	<u>\$ 392,786</u>	<u>\$ —</u>	<u>\$ (346,891)</u>	<u>\$ 45,940</u>
Balance at June 30, 2021	61,920,250	\$ 61	\$ 543,674	\$ (19)	\$ (413,739)	\$ 129,977
Vesting of restricted stock units	22,700	—	—	—	—	—
Stock-based compensation expense	—	—	2,096	—	—	2,096
Other comprehensive gain	—	—	—	14	—	14
Net loss	—	—	—	—	(26,027)	(26,027)
Balance at September 30, 2021	<u>61,942,950</u>	<u>\$ 61</u>	<u>\$ 545,770</u>	<u>\$ (5)</u>	<u>\$ (439,766)</u>	<u>\$ 106,060</u>

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

	Nine Months Ended September 30,	
	2021	2020
Operating activities		
Net loss	\$ (62,745)	\$ (53,908)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	2,050	2,071
Amortization of right-of-use asset	195	196
Stock-based compensation expense	7,479	7,909
Change in fair value of warrant liability	(14,117)	—
Net amortization of premiums and discounts on marketable securities	122	(49)
Amortization of debt-discount and accretion of deferred debt costs	521	196
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(1,813)	(576)
Accounts receivable	7	19,998
Contract assets	(1,308)	(2,152)
Other long-term assets	(694)	(461)
Accounts payable	334	104
Accrued expenses	1,048	70
Deferred revenue	(7,111)	(2,983)
Proceeds for tenant improvement incentive from landlord	—	2,035
Operating lease asset and liabilities	(539)	110
Net cash used in operating activities	<u>(76,571)</u>	<u>(27,440)</u>
Investing activities		
Purchases of property and equipment	(1,000)	(3,307)
Purchases of marketable securities	(51,408)	—
Maturities of marketable securities	—	50,000
Net cash (used in) provided by investing activities	<u>(52,408)</u>	<u>46,693</u>
Financing activities		
Payments on financing lease obligations	(196)	(179)
Proceeds from issuance of common stock through employee benefit plans	157	509
Proceeds from the issuance of common stock through employee stock purchase plan	153	223
Proceeds from issuance of common stock through at-the-market sales agreement, net of issuance costs	—	11,896
Proceeds from term loan, net of issuance costs	—	19,700
Proceeds from issuance of common stock in public offering, net of issuance costs	70,337	—
Payment of issuance cost related to out of period offering	(36)	—
Net cash provided by financing activities	<u>70,415</u>	<u>32,149</u>
Net increase (decrease) in cash, cash equivalents and restricted cash	<u>(58,564)</u>	<u>51,402</u>
Cash, cash equivalents and restricted cash (See reconciliation in Note 6)		
Beginning of period	177,070	44,817
End of period	<u>\$ 118,506</u>	<u>\$ 96,219</u>
Supplemental disclosure of cash flow information:		
Cash paid for interest	\$ 2,380	\$ 1,055
Cash paid for tax	<u>\$ —</u>	<u>\$ 7</u>
Non-cash investing and financing activities:		
Property and equipment received but unpaid as of period end	\$ 178	\$ 139
Offering costs incurred but unpaid as of period end	<u>\$ 10</u>	<u>\$ 103</u>

See accompanying notes to unaudited condensed consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
(unaudited)

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 of 5,400,000 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 September 30, 2021, the Company had an accumulated deficit of \$439.8 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, cash equivalents and marketable securities of \$166.7 million as of September 30, 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 September 30, 2021, the results of its operations, statements of cash flows and statements of stockholders' equity for the three and nine months ended September 30, 2021 and 2020. Such adjustments are of a normal and recurring nature. The results for the three and nine months ended September 30, 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 and corporate debt securities, 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 September 30, 2021, pre-funded warrants to purchase 1,000,000 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 September 30,	
	2021	2020
Stock options	6,264,350	5,549,290
Unvested restricted stock units	1,850,962	1,694,633
Warrants*	4,990,156	2,145,642
Total	13,105,468	9,389,565

* As of September 30, 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 September 30, 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 nine months ended September 30, 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 and nine months ended September 30, 2021, the Company recognized revenue of \$5.6 million and \$12.9 million, respectively, under the GBT Collaboration Agreement. During the three and nine months ended September 30, 2020, the Company recognized revenue of \$3.5 million and \$8.2 million, respectively, under the GBT Collaboration Agreement. As of September 30, 2021, the Company has deferred revenue outstanding under the GBT Collaboration Agreement of approximately \$12.4 million, of which \$9.5 million and \$2.8 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 September 30, 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 and nine months ended September 30, 2021, the Company recognized revenue of \$0.1 million and \$2.8 million, respectively, under the Incyte Collaboration Agreement. During the three and nine months ended September 30, 2020, the Company recognized revenue of \$0.3 million and \$1.2 million, respectively, under the Incyte Collaboration Agreement. As of September 30, 2021, the Company has deferred revenue outstanding under the Incyte Collaboration Agreement of approximately \$2.6 million, of which \$2.5 million and \$0.1 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 nine months ended September 30, 2021 (in thousands):

	Balance at December 31, 2020	Additions	Deductions	Balance at September 30, 2021
Accounts receivable and contract assets:				
Billed receivables from collaboration partners	\$ 7	\$ 7,270	\$ (7,277)	\$ —
Unbilled receivables from collaboration partners	2,324	8,431	(7,123)	3,632
Total accounts receivable and contract assets	<u>\$ 2,331</u>	<u>\$ 15,701</u>	<u>\$ (14,400)</u>	<u>\$ 3,632</u>
Contract liabilities:				
Deferred revenue - Incyte	\$ 5,365	\$ —	\$ (2,766)	\$ 2,599
Deferred revenue - GBT	16,721	145	(4,490)	12,376
Total contract liabilities	<u>\$ 22,086</u>	<u>\$ 145</u>	<u>\$ (7,256)</u>	<u>\$ 14,975</u>

4. Cash, Cash Equivalents and Marketable Securities

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

Cash, cash equivalents and marketable securities consisted of the following at September 30, 2021 and December 31, 2020 (in thousands):

<u>September 30, 2021</u>	<u>Amortized Cost</u>	<u>Unrealized Gains</u>	<u>Unrealized Losses</u>	<u>Fair Value</u>
Cash and cash equivalents:				
Cash and money market funds	\$ 115,420	\$ —	\$ —	\$ 115,420
Marketable securities:				
Corporate debt securities - due in one year or less	30,165	1	(2)	30,164
US Treasury obligation - due in more than one year to five years	11,999	—	(3)	11,996
Corporate debt securities - due in more than one year to five years	9,122	1	(2)	9,121
Total	\$ 166,706	\$ 2	\$ (7)	\$ 166,701

<u>December 31, 2020</u>	<u>Amortized Cost</u>	<u>Unrealized Gains</u>	<u>Unrealized Losses</u>	<u>Fair Value</u>
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 nine months ended September 30, 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.

As of September 30, 2021, marketable securities with maturities of one year or less when purchased are presented in current assets and those with maturities of more than one year are presented in the noncurrent assets in the accompanying condensed consolidated balance sheet.

At September 30, 2021, the Company held eight securities that were in an unrealized loss position. The aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months as of September 30, 2021 was \$23.5 million. There were no securities held by the Company in an unrealized loss position for more than twelve months as of September 30, 2021. The Company has the intent and ability to hold such securities until recovery. The Company determined that there was no material change in the credit risk of the above marketable securities. As a result, the Company determined it did not hold any marketable securities with an other-than temporary impairment as of September 30, 2021.

5. Fair Value Measurements

Assets and liabilities measured at fair value on a recurring basis as of September 30, 2021 and December 31, 2020 were as follows (in thousands):

Description	September 30, 2021	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Cash	\$ 80,371	\$ 80,371	\$ —	\$ —
Money market funds	35,049	35,049	—	—
Corporate debt securities - due in one year or less	30,164	—	30,164	—
US Treasury obligation - due in more than one year to five years	11,996	11,996	—	—
Corporate debt securities - due in more than one year to five years	9,121	—	9,121	—
Total	\$ 166,701	\$ 127,416	\$ 39,285	\$ —
Liabilities:				
Warrant liability	\$ 5,594	\$ —	\$ —	\$ 5,594
Total	\$ 5,594	\$ —	\$ —	\$ 5,594

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	—	—
Total	\$ 173,984	\$ 173,984	\$ —	\$ —
Liabilities:				
Warrant liability	\$ 19,711	\$ —	\$ —	\$ 19,711
Total	\$ 19,711	\$ —	\$ —	\$ 19,711

Assumptions Used in Determining Fair Value of Warrants

The Company issued warrants to purchase an aggregate of up to 2,828,125 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:

	September 30, 2021	December 31, 2020
Stock price	\$ 4.47	\$ 10.85
Risk-free interest rate	0.80 %	0.35 %
Dividend yield	—	—
Expected life (in years)	4.19	4.94
Expected volatility	85.18 %	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 nine months ended September 30, 2021 (in thousands):

Fair value as of December 31, 2020	<u>Warrant liability</u>
	\$ 19,711
Change in fair value	<u>(14,117)</u>
Fair value as of September 30, 2021	\$ 5,594

As of September 30, 2021, the fair value of the long-term debt is based on Level 3 inputs and approximated its carrying value.

6. Restricted Cash

At September 30, 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 September 30, 2021, December 31, 2020, September 30, 2020 and December 31, 2019 (in thousands):

	<u>September 30, 2021</u>	<u>December 31, 2020</u>	<u>September 30, 2020</u>	<u>December 31, 2019</u>
Cash and cash equivalents	\$ 115,420	\$ 173,984	\$ 93,133	\$ 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	<u>\$ 118,506</u>	<u>\$ 177,070</u>	<u>\$ 96,219</u>	<u>\$ 44,817</u>

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 September 30, 2021 (in thousands):

Three months ending December 31, 2021	\$	—
Year ending December 31, 2022		—
Year ending December 31, 2023		16,667
Year ending December 31, 2024		20,000
Year ending December 31, 2025		3,333
Total minimum payments	\$	40,000
Less unamortized debt discount		(507)
Plus accumulated accretion of final fees		579
Less current portion		—
Long-term debt, net of current portion	\$	<u>40,072</u>

For the three and nine months ended September 30, 2021, interest expense related to the Loan Agreement was approximately \$1.0 million and \$2.9 million, respectively. For the three and nine months ended September 30, 2020, interest expense related to the Loan Agreement was approximately \$0.5 million and \$1.2 million, respectively. The total carrying value of debt is classified as long-term on the Company's condensed consolidated balance sheets as of September 30, 2021.

8. Accrued Expenses

Accrued expenses consisted of the following as of September 30, 2021 and December 31, 2020 (in thousands):

	September 30, 2021	December 31, 2020
External research and preclinical development	\$ 7,190	\$ 4,702
Employee compensation and benefits	3,896	5,715
Professional fees	683	602
Facilities and other	70	65
Accrued expenses	<u>\$ 11,839</u>	<u>\$ 11,084</u>

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 \$1.7 million of the lease liability as short-term and \$23.3 million of the lease liability as long-term as of September 30, 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 September 30, 2021 (in thousands):

	<u>Operating</u>	<u>Financing</u>
Three months ending December 31, 2021	\$ 970	\$ 78
Year ending December 31, 2022	3,935	313
Year ending December 31, 2023	4,049	66
Year ending December 31, 2024	4,166	—
Year ending December 31, 2025 and beyond	23,543	—
Total minimum lease payments	36,663	457
Less imputed interest	(11,693)	(32)
Total lease liability	<u>\$ 24,970</u>	<u>\$ 425</u>

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 September 30, 2021 (in thousands):

	<u>Three Months Ended September 30, 2021</u>	<u>Nine Months Ended September 30, 2021</u>
Lease cost:		
Operating lease cost	\$ 772	\$ 2,316
Financing lease cost:		
Amortization of right-of-use asset	\$ 67	\$ 195
Interest on lease liabilities	11	38
Total financing lease cost	<u>\$ 78</u>	<u>\$ 233</u>
Cash paid for amounts included in the measurement of liabilities:		
Operating cash flows from operating lease	\$ 951	\$ 2,853
Operating cash flows from financing lease	\$ 78	\$ 234
Other information:		
Weighted-average remaining lease term (in years) - operating lease		<u>Nine Months Ended September 30, 2021</u> 8.42
Weighted-average discount rate - operating lease		9.30%
Weighted-average remaining lease term (in years) - financing lease		1.56
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. 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 tamibarotene in 2016. In May 2021, the Company paid \$2.0 million to TMRC for a development milestone achieved upon the successful dosing of the first patient in its Phase 3 clinical trial of tamibarotene in MDS patients. In September 2021, 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 tamibarotene in AML patients. 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 tamibarotene 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 tamibarotene that is produced. The Company did not incur any fees under this supply management agreement during the three months ended September 30, 2021 and 2020. The Company incurred \$0.6 million and \$0.8 million under this supply management agreement during the nine months ended September 30, 2021 and 2020, respectively.

10. Stockholders' equity

Issuance of Securities through an Underwritten Public Offering

On January 22, 2021, the Company issued and sold an aggregate of 5,400,000 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 placement 10,312,500 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 September 30, 2021 and December 31, 2020 as \$5.6 million and \$19.7 million, respectively. The change in fair value of \$1.8 million and \$14.1 million was recorded in the condensed statement of operations for the three and nine months ended September 30, 2021, respectively.

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 purchase 1,951,844 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 sold 666 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 into 666,000 shares of common stock. As of September 30, 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 on October 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 September 30, 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 September 30, 2021, 2,737,474 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 September 30, 2021, 2,298,325 shares remained available for future issuance under the 2016 ESPP.

Inducement Grant

During the three and nine months ended September 30, 2021, the Company granted a non-statutory stock option to purchase 360,000 shares of the Company's common stock. This stock option will vest over a four-year period, with 25% of the shares underlying the option award vesting on the one-year anniversary of the applicable employee's employment commencement date and the remaining 75% of the shares underlying each award vesting monthly thereafter for three-years. Vesting of the option is subject to such employee's continued service with the Company through the applicable vesting dates. This stock option was granted outside of the 2016 Plan as an inducement material to the employee's acceptance of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).

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 and nine months ended September 30, 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. None of these performance-based criteria had been achieved or were probable of being achieved as of September 30, 2021; therefore, no expense has been recognized during the three or nine months ended September 30, 2021. There was \$0.3 million of unrecognized compensation cost related to this option, with a remaining contractual period of 5.0 years as of September 30, 2021.

A summary of the status of stock options as of December 31, 2020 and September 30, 2021 and changes during the nine months ended September 30, 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	1,647,000	9.17		
Exercised	(20,134)	7.77		
Cancelled	(831,121)	9.92		
Outstanding at September 30, 2021	<u>6,264,350</u>	\$ 8.84	6.7	\$ 931
Exercisable at September 30, 2021	<u>3,872,773</u>	\$ 9.06	5.4	\$ 931

The intrinsic value of stock options exercised during the nine months ended September 30, 2021 and 2020 was \$0.1 million and \$0.5 million, respectively.

As of September 30, 2021, there was \$12.2 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 2.8 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 September 30, 2021 and changes during the nine months ended September 30, 2021 is presented below:

	Shares	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2020	1,734,383	\$ 7.40
Granted	800,454	9.26
Vested	(267,012)	7.70
Forfeited	(416,863)	7.92
Outstanding at September 30, 2021	<u>1,850,962</u>	<u>\$ 8.04</u>

As of September 30, 2021, there was \$10.4 million of unrecognized stock-based compensation expense related to outstanding restricted stock units, with an expected recognition period of 2.3 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 September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Weighted-average risk-free interest rate	1.12 %	0.46 %	0.87 %	1.29%
Expected dividend yield	— %	— %	— %	— %
Expected option term (in years)	6.06	5.89	6.01	5.99
Volatility	81.24 %	79.96 %	81.88 %	78.26%

The weighted-average grant date fair value per share of options granted in the nine months ended September 30, 2021 and 2020 was \$6.36 and \$5.29, 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 September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Research and development	\$ 1,485	\$ 1,229	\$ 4,260	\$ 3,459
General and administrative	611	1,494	3,219	4,450
Total stock-based compensation expense	<u>\$ 2,096</u>	<u>\$ 2,723</u>	<u>\$ 7,479</u>	<u>\$ 7,909</u>

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:

- tamibarotene, a selective retinoic acid receptor alpha, or RAR α , agonist for which we are conducting SELECT-MDS-1, a Phase 3 clinical trial evaluating tamibarotene in combination with azacitidine in a genomically defined subset of patients with higher-risk myelodysplastic syndrome, or HR-MDS, and for which we are conducting SELECT-AML-1, a randomized Phase 2 clinical trial evaluating tamibarotene 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 are evaluating in a dose confirmation study, and which we plan to follow with 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 plan to evaluate in combination with chemotherapy in pancreatic cancer patients in an expansion cohort of our existing Phase 1 clinical trial, in combination with a Bruton's tyrosine kinase, or BTK, inhibitor in mantle cell lymphoma in a Phase 1b trial, and in combination with atezolizumab, a PD-L1 inhibitor, in BRAF-mutant colorectal cancer in a Phase 1/1b clinical trial sponsored by F. Hoffmann-La Roche AG, or Roche.

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. In 2022, we expect to nominate our next development candidate appropriate for investigational new drug application, or IND, enabling preclinical studies.

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 tamibarotene 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 RAR α 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, tamibarotene 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 associated with resistance to venetoclax. These data suggest that the RARA biomarker not only selects for patients who are more likely to respond to treatment with tamibarotene but also for patients who may be less likely to benefit from treatment with venetoclax. 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.

Based on these data and our assessment of ongoing areas of high unmet need, we are advancing tamibarotene in combination with azacitidine into a registration-enabling Phase 3 clinical trial in RARA-positive newly diagnosed HR-MDS patients, which we refer to as SELECT-MDS-1. 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 tamibarotene in combination with azacitidine or placebo with azacitidine, respectively. The primary endpoint of the trial will be the CR rate. The trial is designed with 90% power and a one-sided alpha of 0.025 to detect a difference in CR rates between the experimental and control arms. We are currently dosing patients in SELECT-MDS-1, 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 are advancing tamibarotene in combination with venetoclax and azacitidine in RARA-positive newly diagnosed unfit AML patients. The trial, which we refer to as SELECT-AML-1, 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 tamibarotene 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 have begun dosing patients in the SELECT-AML-1 trial, 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 have begun dosing patients in a dose confirmation study of SY-2101. The dose confirmation study is evaluating the PK, food effect, safety and tolerability of SY-2101 in up to 24 adult APL patients undergoing consolidation with IV ATO plus ATRA. Participants receive a starting dose of 15 mg of SY-2101 dosed once daily, with flexibility to allow for other doses. Multiple-dose treatments are also being assessed during consolidation to assess steady state PK and safety. We anticipate reporting confirmatory dose and PK data in the first half of 2022. Following confirmation of a dose that demonstrates comparable PK exposures 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.

At the European Society for Medical Oncology Congress held in September 2021, or ESMO 2021, we presented new data from the dose-escalation portion of the Phase 1 multi-center, open-label study of SY-5609 evaluating patients with advanced breast, colorectal, lung, ovarian and pancreatic cancers, as well as patients with solid tumors of any histology harboring Rb pathway alterations. Patients were treated in cohorts exploring continuous daily dosing as well as intermittent dosing regimens, including seven days on treatment and seven days off (7d on/7d off) and five days on treatment and two days off (5d on/2d off). As of a July 6, 2021 data cut-off, 54 patients treated with single-agent SY-5609 in the study were eligible for a safety analysis and 45 patients were evaluable for clinical response. The median age of patients enrolled in the study was 65.5. Patients had been heavily pre-treated with as many as eight prior therapies and a median of four prior therapies. Across all doses and schedules, the majority of adverse events, or AEs, were low-grade and reversible, and there was a low rate of discontinuations due to AEs. The most common treatment-emergent AEs were nausea, diarrhea, thrombocytopenia, fatigue and anemia. Tolerability was optimized with the 7d on/7d off schedule, which had the lowest rates of treatment-emergent AEs, while demonstrating comparable rates of stable disease, or SD, as seen with more dose-intense regimens, supporting the selection of this schedule for further development of SY-5609. The maximum tolerated dose of the 7d on/7d off schedule has not yet been reached as of the data cut-off date. Changes in POLR2A mRNA expression, a pharmacodynamic marker for CDK7 inhibition, were associated with anti-tumor activity and were sustained for at least three days following drug cessation, supporting intermittent dosing. As of the data cut-off date, thirteen patients (29%) had achieved SD, with tumor regressions of up to 20% in six of those patients, across multiple tumor types. The most substantial clinical activity was observed in heavily pre-treated patients with advanced pancreatic cancer, for which five of 13 (39%) evaluable patients achieved SD, with tumor reductions in two of those patients. Further, reductions in the CA 19-9 tumor marker, which is used in clinical practice to monitor tumor progression, were observed in three of four pancreatic cancer patients with serial CA 19-9 data, with these reductions ranging from 32% to 72%. Notably, one metastatic pancreatic cancer patient who had failed two prior lines of therapy and relapsed after a third line of treatment experienced prolonged SD of up to ten months. The analysis of clinical activity by tumor type and mutational status supported the mechanistic rationale for SY-5609 in Rb-altered and KRAS-mutant cancers.

We also presented new preclinical data at ESMO 2021 evaluating the anti-tumor and PD activity of intermittent dosing regimens for SY-5609, as well as new preclinical data evaluating SY-5609 as a single agent and in combination with chemotherapy in pancreatic cancer models. Taken together, these data further support our dose expansion strategy, including the decision to use a 7d on/7d off dosing schedule and combine with chemotherapy in patients with pancreatic cancer.

Based on these data, we intend to further develop SY-5609 by exploring three combination regimens, focusing initially on indications with compelling clinical and/or preclinical activity, as well as a strong mechanistic rationale and high unmet need. We plan to initiate an expansion cohort evaluating SY-5609 in combination with chemotherapy for the treatment of pancreatic cancer in the fourth quarter of 2021. The cohort will enroll patients with metastatic pancreatic cancer who have progressed following first-line treatment with the chemotherapy regimen known as FOLFIRINOX, with one arm exploring a doublet regimen of SY-5609 in combination with gemcitabine and the other arm exploring a triplet regimen of SY-5609 with gemcitabine and nab-paclitaxel. The endpoints for the study are safety and tolerability, as well as efficacy measures, including disease control rate and progression free survival. We also plan to initiate a Phase 1b trial evaluating SY-5609 in combination with a BTK inhibitor for the treatment of mantle cell lymphoma in the first half of 2022. This trial will begin with a safety evaluation of SY-5609 as a single agent, after which we intend to initiate a safety lead-in in combination with a BTK inhibitor in BTK-naïve patients, before moving the combination into a dedicated second-line mantle cell lymphoma patient expansion. The endpoints for this study include safety and tolerability, as well as efficacy measures such as complete response rate, overall response rate and progression-free survival. We plan to employ a 7d on/7d off dosing schedule in both of these trials. In addition, in August 2021, we announced entry into a clinical supply agreement with Roche, pursuant to which we agreed to supply SY-5609 for a combination dosing cohort with atezolizumab in Roche's ongoing Phase 1/1b INTRINSIC trial, which is evaluating multiple targeted therapies or immunotherapy, including atezolizumab, as single agents or in rational specified

combinations in molecularly defined subsets of colorectal cancer patients. SY-5609 will be evaluated in combination with atezolizumab in patients with BRAF-mutant disease. Under the terms of the agreement, Roche will sponsor and conduct the Phase 1/1b study to evaluate the safety, tolerability and preliminary efficacy of the combination of SY-5609 and atezolizumab and will assume all costs associated with the study. In exchange for providing SY-5609, we will receive access to the data on SY-5609 in combination with atezolizumab. We retain all rights to SY-5609.

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 September 30, 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 \$62.7 million and \$53.9 million for the nine months ended September 30, 2021 and 2020, respectively. As of September 30, 2021, we had an accumulated deficit of \$439.8 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 tamibarotene, 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 September 30, 2021 and 2020, we recognized \$5.7 million and \$3.8 million of revenue, of which \$5.6 million and \$3.5 million was related to our collaboration with GBT and \$0.1 million and \$0.3 million to our collaboration with Incyte, respectively. For the nine months ended September 30, 2021 and 2020, we recognized \$15.7 million and \$9.4 million of revenue, of which \$12.9 million and \$8.2 million were related to our collaboration with GBT and \$2.8 million and \$1.2 million were related 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 and nine months ended September 30, 2021 and 2020 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Tamibarotene external costs	\$ 8,464	\$ 4,049	\$ 22,028	\$ 9,204
SY-5609 and other CDK7 program external costs (1)	2,650	2,994	8,576	8,483
SY-2101 program external costs	1,277	—	3,035	—
Other research and platform program external costs	5,564	3,182	12,797	7,962
Employee-related expenses, including stock-based compensation	7,515	5,847	21,596	16,703
Facilities and other expenses	1,792	1,602	5,045	4,687
Total research and development expenses	\$ 27,262	\$ 17,674	\$ 73,077	\$ 47,039

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- (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 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 2020 10-K.

Results of Operations

Comparison of three months ended September 30, 2021 and 2020

The following table summarizes our results of operations for the three months ended September 30, 2021 and 2020, together with the changes in those items in dollars (in thousands):

	Three Months Ended September 30,		Dollar Change	% Change
	2021	2020		
Statements of Operations Data:				
Revenue	\$ 5,697	\$ 3,828	\$ 1,869	49 %
Operating expenses:				
Research and development	27,262	17,674	9,588	54 %
General and administrative	5,346	5,151	195	4 %
Total operating expenses	32,608	22,825	9,783	43 %
Loss from operations	(26,911)	(18,997)	(7,914)	42 %
Interest income	32	4	28	700 %
Interest expense	(984)	(493)	(491)	100 %
Change in fair value of warrant liability	1,836	—	1,836	— %
Net loss	\$ (26,027)	\$ (19,486)	\$ (6,541)	34 %

Revenue

For the three months ended September 30, 2021, revenue was \$5.7 million, of which \$5.6 million was attributable to our collaboration with GBT and \$0.1 million was attributable to our collaboration with Incyte. For the three months ended September 30, 2020, revenue was \$3.8 million, of which \$3.5 million was attributable to our collaboration with GBT and \$0.3 million was attributable to our collaboration with Incyte.

Research and Development Expense

Research and development expense increased by approximately \$9.6 million, or 54%, from \$17.7 million for the three months ended September 30, 2020 to \$27.3 million for the three months ended September 30, 2021. The following table summarizes our research and development expenses for the three months ended September 30, 2021 and 2020, together with the changes to those items in dollars (in thousands):

	Three Months Ended September 30,		Dollar Change	% Change
	2021	2020		
External research and development	\$ 15,907	\$ 9,333	\$ 6,574	70 %
Employee-related expenses, excluding stock-based compensation	6,030	4,618	1,412	31 %
Stock-based compensation	1,485	1,229	256	21 %
Consulting, licensing and professional fees	2,048	892	1,156	130 %
Facilities and other expenses	1,792	1,602	190	12 %
Total research and development expenses	<u>\$ 27,262</u>	<u>\$ 17,674</u>	<u>\$ 9,588</u>	<u>54 %</u>

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 \$6.6 million, or 70%, for external research and development costs, primarily due to increases 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 \$1.4 million, or 31%, for employee-related expenses, including increased salary and benefits, primarily due to our increased headcount;
- an increase of approximately \$0.3 million, or 21%, for stock-based compensation expense, also primarily due to our increased headcount;
- an increase of approximately \$1.2 million, or 130%, for consulting, licensing and professional fees, primarily related to the advancement of our clinical and pre-clinical programs; and
- an increase of approximately \$0.2 million, or 12%, for facilities and other expenses, primarily due to our increased headcount.

General and Administrative Expense

General and administrative expense increased by approximately \$0.2 million, or 4%, from \$5.2 million for the three months ended September 30, 2020 to \$5.3 million for the three months ended September 30, 2021. The change in general and administrative expense was primarily attributable to an increase in employee-related expenses driven by increased headcount, an increase in legal costs including patent prosecution expenses, and an increase in consulting fees.

Interest Income

Interest income was derived generally from our investments in cash, cash equivalents, and marketable securities. The increase in interest income during the three months ended September 30, 2021 as compared to the three months ended September 30, 2020 was due to an increase in our investments in these securities during the period ended September 30, 2021.

Interest Expense

Interest expense was related to our credit facility with Oxford and equipment financing arrangements. Interest expense increased by approximately \$0.5 million, or 100%, from \$0.5 million for the three months ended September 30, 2020 to \$1.0 million for the three months ended September 30, 2021. The increase in interest expense during the three months ended September 30, 2021 as compared to the three months ended September 30, 2020 was driven by an

increase in outstanding debt during the three months ended September 30, 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 three months ended September 30, 2021. Interest expense during the three months ended September 30, 2020 was based only on the first tranche of \$20.0 million that was drawn in February 2020.

Change in Fair Value of Warrant Liability

The change in fair value of warrant liability during the three months ended September 30, 2021 as compared to the three months ended September 30, 2020 was a result of the remeasurement of the fair value of warrants issued in connection with the December 2020 private placement.

Comparison of nine months ended September 30, 2021 and 2020

The following table summarizes our results of operations for the nine months ended September 30, 2021 and 2020, together with the changes in those items in dollars (in thousands):

	Nine Months Ended September 30,		Dollar Change	% Change
	2021	2020		
Statements of Operations Data:				
Revenue	\$ 15,686	\$ 9,394	\$ 6,292	67 %
Operating expenses:				
Research and development	73,077	47,039	26,038	55 %
General and administrative	16,606	15,433	1,173	8 %
Total operating expenses	89,683	62,472	27,211	44 %
Loss from operations	(73,997)	(53,078)	(20,919)	39 %
Interest income	56	421	(365)	(87) %
Interest expense	(2,921)	(1,251)	(1,670)	133 %
Change in fair value of warrant liability	14,117	—	14,117	— %
Net loss	<u>\$ (62,745)</u>	<u>\$ (53,908)</u>	<u>\$ (8,837)</u>	<u>16 %</u>

Revenue

For the nine months ended September 30, 2021, revenue was \$15.7 million, of which \$12.9 million was attributable to our collaboration with GBT and \$2.8 million was attributable to our collaboration with Incyte. For the nine months ended September 30, 2020, revenue was \$9.4 million, of which \$8.2 million was attributable to our collaboration with GBT and \$1.2 million was attributable to our collaboration with Incyte.

Research and Development Expense

Research and development expense increased by approximately \$26.0 million, or 55%, from \$47.0 million for the nine months ended September 30, 2020 to \$73.1 million for the nine months ended September 30, 2021. The following table summarizes our research and development expenses for the nine months ended September 30, 2021 and 2020, together with the changes to those items in dollars (in thousands):

	Nine Months Ended September 30,		Dollar Change	% Change
	2021	2020		
External research and development	\$ 41,726	\$ 23,074	\$ 18,652	81 %
Employee-related expenses, excluding stock-based compensation	17,336	13,244	4,092	31 %
Stock-based compensation	4,260	3,459	801	23 %
Consulting, licensing and professional fees	4,710	2,575	2,135	83 %
Facilities and other expenses	5,045	4,687	358	8 %
Total research and development expenses	<u>\$ 73,077</u>	<u>\$ 47,039</u>	<u>\$ 26,038</u>	<u>55 %</u>

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 \$18.7 million, or 81%, for external research and development costs, primarily due to increases 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 \$4.1 million, or 31%, for employee-related expenses, including increased salary and benefits, primarily due to our increased headcount;
- an increase of approximately \$0.8 million, or 23%, for stock-based compensation expense, also primarily due to our increased headcount;
- an increase of approximately \$2.1 million, or 83%, for consulting, licensing and professional fees primarily related to the advancement of our clinical and pre-clinical programs; and
- an increase of approximately \$0.4 million, or 8%, for facilities and other expenses, primarily due to our increased headcount.

General and Administrative Expense

General and administrative expense increased by approximately \$1.2 million, or 8%, from \$15.4 million for the nine months ended September 30, 2020 to \$16.6 million for the nine months ended September 30, 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 employees, an increase in legal costs including patent prosecution expenses, and an increase in consulting fees.

Interest Income

Interest income was derived generally from our investments in cash, cash equivalents, and marketable securities. The decrease in interest income during the nine months ended September 30, 2021 as compared to the nine months ended September 30, 2020 was due to lower yield on our investments in these securities due to capital market conditions during the nine months ended September 30, 2021.

Interest Expense

Interest expense was related to our credit facility with Oxford and equipment financing arrangements. Interest expense increased by approximately \$1.7 million, or 133%, from \$1.3 million for the nine months ended September 30, 2020 to \$2.9 million for the nine months ended September 30, 2021. The increase in interest expense during the nine months ended September 30, 2021 as compared to the nine months ended September 30, 2020 was driven by an increase in outstanding debt during the nine months ended September 30, 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 nine months ended September 30, 2021. Interest expense during the nine months ended September 30, 2020 was based only on the first tranche of \$20.0 million that was drawn in February 2020.

Change in Fair Value of Warrant Liability

The change in fair value of warrant liability during the nine months ended September 30, 2021 as compared to the nine months ended September 30, 2020 was a result of the remeasurement of the fair value of warrants issued in connection with the December 2020 private placement.

Liquidity and Capital Resources

Sources of Liquidity

We funded our operations from inception through September 30, 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 September 30, 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 September 30, 2021, \$75.0 million in common stock remained available for future issuance under the sales agreement.

As of September 30, 2021, \$224.4 million of securities remained available for future issuance under the shelf registration statement.

As of September 30, 2021, we had cash, cash equivalents, and marketable securities of approximately \$166.7 million.

Cash Flows

The following table provides information regarding our cash flows for the nine months ended September 30, 2021 and 2020 (in thousands):

	Nine Months Ended September 30,	
	2021	2020
Net cash (used in) provided by:		
Operating activities	\$ (76,571)	\$ (27,440)
Investing activities	(52,408)	46,693
Financing activities	70,415	32,149
Net (decrease) increase in cash, cash equivalents and restricted cash	<u>\$ (58,564)</u>	<u>\$ 51,402</u>

Net Cash Used in Operating Activities

Net cash used in operating activities for the nine months ended September 30, 2021 and 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 \$76.6 million during the nine months ended September 30, 2021 compared to \$27.4 million for the nine months ended September 30, 2020. The increase in net cash used in operating activities during the nine months ended September 30, 2021 was primarily due to a \$21.1 million increase in loss from operations during the nine months ended September 30, 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 nine months ended September 30, 2021.

Net Cash (Used in) Provided by Investing Activities

Net cash used in investing activities was \$52.4 million during the nine months ended September 30, 2021 compared to net cash provided by investing activities of \$46.7 million during the nine months ended September 30, 2020. The decrease in net cash provided by investing activities was primarily due to maturities of marketable securities of \$50.0 million, offset by the purchase of \$3.3 million of property and equipment during the nine months ended September 30, 2020, as compared to \$1.0 million in the nine months ended September 30, 2021, and purchases of marketable securities of \$51.4 million during the nine months ended September 30, 2021.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was \$70.4 million during the nine months ended September 30, 2021 compared to \$32.1 million for the nine months ended September 30, 2020. Cash provided by financing activities for the nine months ended September 30, 2021 was primarily due to net proceeds of \$70.3 million from a public offering of shares of our common stock, \$0.2 million of proceeds from the issuance of common stock under our employee stock purchase plan, and \$0.2 million of proceeds from the exercise of stock options, offset by \$0.2 million of payments made under our finance lease. In comparison, the cash provided by financing activities for the nine months ended September 30, 2020 was primarily due to \$11.9 million of net proceeds from the issuance of shares of our common stock pursuant to the 2017 sales agreement with Cowen, \$19.7 million of net proceeds from the first tranche of the Oxford loan, \$0.2 million of proceeds from the issuance of common stock under our employee stock purchase plan, and \$0.5 million of proceeds from the exercise of stock options, offset by \$0.2 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 tamibarotene, 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, cash equivalents, and marketable securities as of September 30, 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 tamibarotene, 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 tamibarotene;
- 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 cash equivalents and marketable securities primarily consist of money market funds that invest in U.S. Treasury obligations, as well as corporate debt securities. 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 primarily in the form of money market funds and are invested in U.S. treasury or government obligations. However, because of 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 September 30, 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 nine-month periods ended September 30, 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 September 30, 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 pandemics, 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, epidemics and 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 pandemic, 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. We have eased these restrictions over time in accordance with guidance from applicable governmental authorities. 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 are monitoring the potential impact of surges of COVID-19 cases in jurisdictions where our contract manufacturing organization partners and clinical sites are located. 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 positive 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 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, which may be adversely impacted by a remote work environment, 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 newly diagnosed AML or patient subsets within newly diagnosed AML (including ivosidenib, venetoclax and glasdegib), and one new drug approved by the FDA in 2020 for the treatment of MDS or patient subsets within MDS (decitabine/cedazuridine). Tamibarotene may also face competition from other agents currently in clinical development for AML and MDS, including those in late-stage development from Takeda Pharmaceutical Co. Ltd., Gilead Sciences, Inc., Abbvie Inc., Roche Holding AG, Novartis AG, Astex Pharmaceuticals, Inc., and Pfizer Inc.

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 by Phebra Pty Ltd, or Phebra, an Australian based specialty pharmaceutical group. Phebra has entered into an agreement with Medsenic SAS, a European biopharmaceutical company, for the investigation of their oral arsenic trioxide compound for the treatment of autoimmune diseases. We are also aware 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. and Exelixis, Inc., 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, and a collaboration between Exscientia Ltd. and GT Apeiron Therapeutics Ltd. focused on developing novel CDK inhibitors, including selective CDK7 inhibitors. SY-5609 may face competition from these CDK7 inhibitors. There is also significant competition from products with mechanisms other than CDK7 inhibition in pancreatic cancer, mantle cell lymphoma and BRAF-mutant colorectal cancer, the disease areas where we are currently focusing our development of SY-5609. 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 tamibarotene, which in turn will impact the potential return on investments in clinical trials of tamibarotene. 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.

If we are to receive FDA approval for SY-2101 prior to January 2025, we must demonstrate to the FDA that SY-2101 provides a “major contribution to patient care” relative to an approved drug with the same active moiety for the same indication, and there can be no assurance that we will be successful.

We are developing SY-2101 as an alternative to Trisenox®, an intravenously administered arsenic trioxide product. The FDA has granted Trisenox orphan drug exclusivity for the treatment of a form of APL until January 2025. A company that obtains FDA approval for a designated orphan drug receives orphan drug market exclusivity for the designated indication for a period of seven years from the date of approval in the United States. This orphan drug exclusivity approval bars the FDA from approving another drug product with the same active moiety for the same orphan drug indication, unless the sponsor of the drug product is able to demonstrate, and the FDA concludes, that the drug product is “clinically superior” to the previously approved product, due to the fact that it is safer, more effective, or provides a major contribution to patient care within the meaning of FDA regulations and guidance.

In assessing whether a sponsor has demonstrated that its candidate product provides a “major contribution to patient care” when compared to the drug product with orphan drug exclusivity, the FDA will evaluate the question on a case by case basis and may in appropriate circumstances consider such factors as convenience of treatment location, duration of treatment, patient comfort, reduced treatment burden, advances in ease and comfort of drug administration, longer periods between doses, and the potential for self-administration of the product. Such demonstration to the satisfaction of the FDA is difficult to establish with limited precedents.

SY-2101 was granted an orphan drug designation by the FDA for the treatment of APL in November 2015, after the FDA concluded that there is a plausible hypothesis for clinical superiority when compared to Trisenox. Specifically, given that SY-2101 is administered orally instead of intravenously, it could provide a major contribution to patient care by allowing for the treatment of APL patients in a more convenient outpatient setting through a self-administered delivery method, which could eliminate or significantly decrease the costs associated with IV administration, reduce the inconvenience and cost to patients and caregivers associated with frequent hospitalizations and trips to infusion centers, and reduce the burden on the healthcare system in delivery of life-saving medicines to patients in need. We intend to seek to demonstrate to the FDA that SY-2101 is “clinically superior” to Trisenox.

constituting a “major contribution to patient care” within the meaning of the FDA regulations and guidance. However, there can be no assurance that we will be successful in these efforts and, if we are not, the FDA will not approve SY-2101 until orphan drug exclusivity expires for Trisenox. Similarly, if a competitor were to obtain FDA approval for an oral arsenic trioxide product in APL before we do in that indication, in order to obtain FDA approval, we would need to demonstrate that SY-2101 is clinically superior to that competing product, which may be difficult in the case of another oral agent with an efficacy profile comparable to Trisenox. Any failure to demonstrate “clinical superiority” for SY-2101 could prevent or delay FDA approval or cause SY-2101 to fail to receive or maintain orphan drug exclusivity status, which could have a material adverse effect on our business, prospects, financial condition and results of operations.

Item 6. Exhibits.

<u>Exhibit No.</u>	<u>Description of Exhibit</u>
3.1	<u>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).</u>
3.2	<u>Second Amended and Restated By-Laws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2021 (File No. 001-37813) filed on August 5, 2021).</u>
10.1*	<u>Form of Nonstatutory Stock Option Agreement for Inducement Awards (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on October 13, 2021).</u>
10.2*	<u>Offer Letter, effective September 27, 2021, between Syros Pharmaceuticals, Inc. and Conley Chee. Filed herewith.</u>
10.3*	<u>Offer Letter, effective October 12, 2021, between Syros Pharmaceuticals, Inc. and Jason Haas (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on October 13, 2021).</u>
31.1	<u>Certification of principal executive officer pursuant to Rule 13a-14(a), promulgated under the Securities Exchange Act of 1934, as amended.</u>
31.2	<u>Certification of principal financial officer pursuant to Rule 13a-14(a), promulgated under the Securities Exchange Act of 1934, as amended.</u>
32.1	<u>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.</u>
32.2	<u>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.</u>
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)

* Indicates management contract or compensatory plan.

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.

Date: November 5, 2021

Syros Pharmaceuticals, Inc.

By: /s/ Jason Haas

Jason Haas

Chief Financial Officer (Principal Financial Officer)



September 10, 2021

Conley Chee
Delivered via Email

Dear Conley:

On behalf of Syros Pharmaceuticals, Inc. (the “**Company**”), I am pleased to extend the following offer and set forth the terms of your employment with the Company:

1. You will be employed to serve on a full-time basis as Chief Commercial Officer, effective September 27, 2021. As Chief Commercial Officer, you will report to the Company’s President and Chief Executive Officer, who is currently Nancy Simonian, and be responsible for leading all aspects of the Company’s commercial initiatives, playing a key role in the Company’s strategic planning process, and such other duties as may from time to time be assigned to you by the Company.
2. Your salary will be \$440,000 per year, paid bi-weekly in arrears in accordance with the Company’s normal payroll processes and subject to tax and other withholdings as required by law. Such salary may be adjusted from time to time in accordance with normal business practice and in the sole discretion of the Company. You will receive performance reviews in accordance with the Company’s standard practice for executive officers.
3. You may participate in any and all bonus and benefit programs that the Company establishes and makes available to its employees from time to time, provided you are eligible to participate in such programs as provided under (and subject to all provisions of) the plan documents governing those programs. Subject to the approval of the Company’s Board of Directors or a committee of the Board of Directors (the “**Board**”), you will be eligible to receive a discretionary cash bonus award based on your individual and the Company’s performance during the applicable fiscal year (or portion thereof) as determined by the Company in its sole discretion. Your target bonus will be 40% of your base salary. You must be an active employee of the Company on the date bonuses are paid in order to be eligible for a discretionary bonus award. Future bonus eligibility will be based on the terms and conditions of the Company’s discretionary cash bonus program prevailing at that time. The bonus and benefit programs made available by the Company, and the rules, terms and conditions for participation in such benefit plans, may be changed by the Company at any time without advance notice.



4. Without otherwise limiting the “at-will” nature of your employment, in the event your employment is terminated by the Company without Cause or by you for Good Reason, you shall be entitled to the base salary that has accrued and to which you are entitled as of the effective date of such termination, and further, subject to the conditions set forth in the second paragraph of this Section 5, the Company shall, for a period of nine (9) months following your termination date: (i) continue to pay you, in accordance with the Company’s regularly established payroll procedure, your base salary as severance; and (ii) provided you are eligible for and timely elect to continue receiving group medical insurance pursuant to the “COBRA” law, continue to pay the share of the premium for health coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage, unless the Company’s provision of such COBRA payments will violate the nondiscrimination requirements of applicable law, in which case this benefit will not apply. If, within the three months prior to a Change in Control or in the twelve months following a Change in Control, the Company terminates your employment without Cause or you resign for Good Reason, the Company, subject to the conditions set forth in the second paragraph of this Section 5, will: (a) extend the severance benefits described in (i) and (ii) above for an additional three months, such that the total severance benefit period shall be one (1) year; (b) pay you a lump sum amount equal to your target bonus in effect for the fiscal year in which your separation from employment occurs; and (c) accelerate the vesting of all unvested stock options held by you as of the date your employment is terminated such that 100% of such options shall become fully vested and exercisable effective as of such date.

Notwithstanding the foregoing, you will not be entitled to receive any severance benefits unless, within sixty (60) days following the date of termination, you (i) have executed a severance and release of claims agreement in a form prescribed by the Company or persons affiliated with the Company (which will include, at a minimum, a release of all releasable claims and non-disparagement and cooperation obligations). Any severance payments shall be paid, or commence on the first payroll period following the date the release becomes effective. Notwithstanding the foregoing, if the 60th day following the date of termination occurs in the calendar year following the calendar year of the termination, then the severance payments shall commence in such subsequent calendar year, and further provided that if such payments commence in such subsequent calendar year, the first such payment shall be a lump sum in an amount equal to the payments that would have come due since your separation from service.

For purposes of this Agreement, “**Change in Control**” means any transaction or series of related transactions (a) the result of which is a change in the ownership of the Company, such that more than 50% of the equity securities of the Company are acquired by any person or group (as such terms are defined for purposes of Section 13(d)(3) of the Securities Exchange Act of 1934, as amended) that does not own capital stock of the Company of the effective date of such change in control, (b) that results in the sale of all or substantially all of the assets of the Company, or (c) that results in the consolidation or merger of the Company with or into another corporation or corporations or other entity in which the Company is not the survivor (except any such corporation or entity controlled, directly or indirectly, by the Company).

“**Cause**” means: (a) your conviction of, or plea of guilty or nolo contendere to, any crime involving dishonesty or moral turpitude or any felony; or (b) you have (i) engaged in material dishonesty, willful misconduct or gross negligence, (ii) breached or threatened to breach either or both of the Non-Disclosure, Assignment and Non-Solicitation Agreement (as described below), (iii) materially violated a Company policy or procedure causing or threatening to cause substantial injury to the Company, and/or (iv) willfully refused to perform your assigned duties to the Company, following written notice by the Company of such breach, violation or refusal as set forth in (ii), (iii) and/or (iv) and a period of thirty (30) days to cure the same.

“**Good Reason**” means the occurrence of one or more of the following without your written consent: (a) a material reduction in your authority, duties and/or responsibilities as compared to your authority, duties and/or responsibilities in effect immediately prior to the occurrence of the event (for example, but not by way of limitation, this determination will include an analysis of whether you maintain at least the same level, scope and type of duties and responsibilities with respect to the management, strategy, operations and business of the Company), (b) a material reduction in your base compensation as compared to your base compensation in effect immediately prior to the occurrence of the event, or (c) the relocation of your principal business location to a location more than 50 miles from your then-current business location; provided, however, that no such occurrence shall constitute Good Reason unless: (i) you give the Company a written notice of termination for Good Reason not more than ninety (90) days after the initial existence of the condition, (ii) the grounds for termination (if susceptible to correction) are not corrected by the Company within thirty (30) days of its receipt of such notice, and (iii) your termination of employment occurs within one (1) year following the Company’s receipt of such notice.

Subject to the approval of the Board or its designee, the Company will grant to you a stock option (the “**Option**”) for the purchase of 360,000 shares of common stock of the Company (“**Common Stock**”), at a price per share equal to the closing price of the Common Stock on the date of grant of such Option. The Option shall vest (i) as to 25% of the shares underlying the option on the one-year anniversary of your first day of employment, and (ii) as to the remaining shares underlying the option in equal monthly installments for the next 36 months thereafter, becoming fully vested on the fourth anniversary of your first day of employment, provided that you remain employed by us on the applicable vesting date. The Option will be granted pursuant to the inducement grant exception under NASDAQ Rule 5635(c)(4) and not pursuant to the Company’s 2016 Stock Incentive Plan or any other equity incentive plan of the Company, as an inducement that is material to your entering into employment with the Company. This Option shall also be subject to such other terms and conditions of the applicable Stock Option Agreement.

You may be eligible to receive such future long-term incentive awards as the Board shall deem appropriate.

5. You will be required to execute a Non-Disclosure, Assignment and Non-Solicitation Agreement in the form attached as Exhibit A as a condition of employment. Upon your appointment by the Board of Directors as an “executive officer” of the Company, the

Company will enter into an indemnification agreement with you in the form currently approved by the Board of Directors.

6. Except as previously disclosed in writing to the Company, you represent that you are not bound by any employment contract, restrictive covenant or other restriction preventing you from entering into employment with or carrying out your responsibilities for the Company, or which is in any way inconsistent with the terms of this letter.

7. You agree to provide to the Company, within three days of your hire date, documentation of your eligibility to work in the United States, as required by the Immigration Reform and Control Act of 1986. You may need to obtain a work visa in order to be eligible to work in the United States. If that is the case, your employment with the Company will be conditioned upon your obtaining a work visa in a timely manner as determined by the Company.

8. This letter shall not be construed as an agreement, either expressed or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at will, under which both you and the Company remain free to terminate the employment relationship, with or without cause, at any time, with or without notice. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company.

9. This letter is intended to provide payments that are exempt from or compliant with Section 409A (as defined in Attachment A), and should be interpreted consistent with that intent.

If you agree with the employment provisions of this letter, please sign the letter and exhibits, scan the signature pages and email to Lisa Roberts at lroberts@syros.com. If you do not accept this offer by September 15, 2021, this offer will be revoked.

Very Truly Yours,

By: /s/ Nancy Simonian
Name: Nancy Simonian
Title: Chief Executive Officer

The foregoing correctly sets forth the terms of my employment by Syros Pharmaceuticals, Inc.

/s/ Conley Chee
Conley Chee

Date: Sept 12, 2021

Attachment A

Payments Subject to Section 409A

- 1) Subject to this Attachment A, any severance payments that may be due under the letter agreement shall begin only upon the date of your “separation from service” (determined as set forth below) which occurs on or after the termination of your employment. The following rules shall apply with respect to distribution of the severance payments, if any, to be provided to you under the letter agreement, as applicable:
 - a) It is intended that each installment of the severance payments under the letter agreement provided under the letter agreement shall be treated as a separate “payment” for purposes of Section 409A of the Internal Revenue Code of 1986, as amended (“Section 409A”). Neither the Company nor you shall have the right to accelerate or defer the delivery of any such payments except to the extent specifically permitted or required by Section 409A.
 - b) If, as of the date of your “separation from service” from the Company, you are not a “specified employee” (within the meaning of Section 409A), then each installment of the severance payments shall be made on the dates and terms set forth in the letter agreement.
 - c) If, as of the date of your “separation from service” from the Company, you are a “specified employee” (within the meaning of Section 409A), then:
 - i) Each installment of the severance payments due under the letter agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when your separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1 (b)(4) to the maximum extent permissible under Section 409A and shall be paid on the dates and terms set forth in the letter agreement; and
 - ii) Each installment of the severance payments due under the letter agreement that is not described in this Attachment A, Section 1(c)(i) and that would, absent this subsection, be paid within the six-month period following your “separation from service” from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, your death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following your separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of payments if and to the maximum extent that that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the
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last day of your second taxable year following the taxable year in which the separation from service occurs.

- 2) The determination of whether and when your separation from service from the Company has occurred shall be made and in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1 (h). Solely for purposes of this Attachment A, Section 2, "Company" shall include all persons with whom the Company would be considered a single employer under Section 414(b) and 414(c) of the Internal Revenue Code of 1986, as amended.
 - 3) The Company makes no representation or warranty and shall have no liability to you or to any other person if any of the provisions of the letter agreement (including this Attachment) are determined to constitute deferred compensation subject to Section 409A but that do not satisfy an exemption from, or the conditions of, that section.
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Exhibit A

Non-Disclosure, Assignment and Non-Solicitation Agreement

NON-DISCLOSURE, ASSIGNMENT AND NON-SOLICITATION AGREEMENT

This Agreement is made by and between Syros Pharmaceuticals, Inc., a Delaware corporation (together with its subsidiaries, successors, and assigns, “**Syros**”), and Conley Chee (“**you**”). In consideration of your employment or continued employment by Syros, and other good and valuable consideration that you agree is fair and reasonable, you and Syros hereby agree as follows:

1. **Condition of Employment.** You acknowledge that your employment and/or the continuation of that employment with Syros is contingent upon your agreement to sign and adhere to the provisions of this Agreement. You further acknowledge that the nature of Syros’ business is such that protection of its proprietary and confidential information is critical to its survival and success.

2. **Proprietary and Confidential Information.**

(a) You agree that all information and know-how, including negative know-how, whether or not in writing, of a private, secret or confidential nature concerning Syros’s business or financial affairs (collectively, “**Proprietary Information**”) is and shall be the exclusive property of Syros. By way of illustration, but not limitation, Proprietary Information may include discoveries, inventions, products, product improvements, product enhancements, processes, methods, techniques, formulas, compositions, compounds, negotiation strategies and positions, projects, developments, plans (including business and marketing plans), research data, clinical data, financial data (including sales costs, profits, pricing methods), personnel data, computer programs (including software used pursuant to a license agreement), customer, prospect and supplier lists, and contacts at or knowledge of customers or prospective customers of Syros. You will not disclose any Proprietary Information to any person or entity other than employees of Syros or use the same for any purposes (other than in the performance of your duties as an employee of Syros) without written approval by an officer of Syros, either during or after your employment with Syros, unless and until such Proprietary Information has become public knowledge without fault by you or anyone acting on your behalf. While employed by Syros, you will use your best efforts to prevent unauthorized publication or disclosure of any of Syros’ Proprietary Information.

(b) You agree that all files, documents, letters, e-mails, text messages, instant messages, memoranda, notes, reports, records, data, sketches, drawings, models, laboratory notebooks, program listings, computer equipment or devices, computer programs or other written, photographic, or other tangible or intangible material containing Proprietary Information, whether created by you or others, which shall come into your custody or possession, shall be and are the exclusive property of Syros, to be used by you only in the performance of your duties for Syros and shall not be copied or removed from Syros’ premises except in the pursuit of the business of Syros. All such materials or copies thereof and all tangible property of Syros in your custody or possession shall be delivered to Syros, upon the earlier of (i) a request by Syros or (ii) immediately upon termination of your employment. After such delivery, you shall not retain any such materials or copies thereof or any such tangible property.

(c) You agree that your obligation not to disclose or to use information and materials of the types set forth in paragraphs 2(a) and 2(b) above, and your obligation to return materials and tangible property set forth in paragraph 2(b) above, also extends to such types of information, materials and tangible property of customers of Syros or suppliers to Syros or other third parties who may have disclosed or entrusted the same to Syros or to you in the course of Syros’ business.

(d) Notwithstanding the provisions of (a)-(c) above, nothing in this Agreement prohibits you from communicating with government agencies about possible violations of federal, state,

or local laws or otherwise providing information to government agencies or participating in government agency investigations or proceedings. You are not required to notify Syros of any such communications; *provided, however*, that nothing herein authorizes the disclosure of information you obtained through a communication that was subject to the attorney-client privilege. Further, notwithstanding your confidentiality and nondisclosure obligations, you are hereby advised as follows pursuant to the Defend Trade Secrets Act: “*An individual shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal. An individual who files a lawsuit for retaliation by an employer for reporting a suspected violation of law may disclose the trade secret to the attorney of the individual and use the trade secret information in the court proceeding, if the individual (A) files any document containing the trade secret under seal; and (B) does not disclose the trade secret, except pursuant to court order.*”

3. **Developments.**

(a) You will make full and prompt disclosure to Syros of all discoveries, inventions, improvements, enhancements, processes, methods, techniques, developments, software, and works of authorship, whether patentable or not, that are created, made, conceived or reduced to practice by you or under your direction or jointly with others during your employment by Syros, whether or not during normal working hours or on the premises of Syros (all of which are collectively referred to in this Agreement as “**Developments**”).

(b) You agree to assign and do hereby assign to Syros (or any person or entity designated by Syros) all of your right, title and interest in and to all Developments and all related patents, patent applications, copyrights and copyright applications. This paragraph 3(b) shall not apply, however, to Developments that are wholly unrelated to the business or research and development conducted or planned to be conducted by Syros at the time such Development is created, made, conceived or reduced to practice and which are made and conceived by you (i) outside of normal working hours, (ii) other than on Syros’s premises, and (iii) not using Syros’ tools, devices, equipment or Proprietary Information. You understand that, to the extent this Agreement shall be construed in accordance with the laws of any state that precludes a requirement in an employee agreement to assign certain classes of inventions made by an employee, this paragraph 3(b) shall be interpreted not to apply to any invention which a court rules and/or Syros agrees falls within such classes. You also hereby waive all claims to moral rights in any Developments.

(c) You agree to cooperate fully with Syros, both during and after your employment with Syros, with respect to the procurement, maintenance and enforcement of copyrights, patents and other intellectual property rights (both in the United States and foreign countries) relating to Developments. You shall sign all papers, including, without limitation, copyright applications, patent applications, declarations, oaths, formal assignments, assignments of priority rights, and powers of attorney, which Syros may deem necessary or desirable in order to protect its rights and interests in any Development. You further agree that if Syros is unable, after reasonable effort, to secure your signature on any such papers, any executive officer of Syros shall be entitled to execute any such papers as your agent and attorney-in-fact, and you hereby irrevocably designate and appoint each executive officer of Syros as your agent and attorney-in-fact to execute any such papers on your behalf, and to take any and all actions as Syros may deem necessary or desirable in order to protect its rights and interests in any Development under the conditions described in this sentence.

4. **Non-Solicitation.** While you are employed by Syros and for a period of 12 months after the termination or cessation of such employment for any reason, you will not directly or indirectly:

(a) Either alone or in association with others, solicit, divert, take away, or accept, or attempt to divert or take away, the business or patronage of any of the actual or prospective clients, customers, or business partners of Syros that were contacted, solicited, or served by Syros during the 12-month period prior to the termination or cessation of your employment with Syros, or about which you became aware and/or obtained confidential information as a result of your employment with Syros; or

(b) Either alone or in association with others (i) solicit, induce or attempt to induce, any employee or independent contractor of Syros to terminate his or her employment or other engagement with Syros, or (ii) hire, or recruit or attempt to hire, or engage or attempt to engage as an independent contractor, any person who was employed or otherwise engaged by Syros at any time during the term of your employment with Syros; *provided* that clause (ii) of this paragraph shall not apply to the recruitment or hiring or other engagement of any individual whose employment or other engagement with Syros has been terminated for a period of six months or longer.

(c) Extension. If you violate the provisions of any of the preceding paragraphs of this Section 4, you shall continue to be bound by the restrictions set forth in such paragraph until a period of 12 months has expired without any violation of such provisions.

(d) Interpretation. If any restriction set forth in Section 4 is found by any court of competent jurisdiction to be unenforceable because it extends for too long a period of time or over too great a range of activities or in too broad a geographic area, it shall be reformed and interpreted to extend only over the maximum period of time, range of activities or geographic area as to which it may be enforceable.

(e) Change in Position. You acknowledge and agree that any change, whether material or immaterial, to the terms of your engagement, or your position, title, duties, salary, benefits, and/or compensation with Syros, shall not cause this Agreement to terminate and shall not affect Employee's obligations under this Agreement, or affect the validity or enforceability of this Agreement.

5. **Other Agreements**. You represent that, except as you has disclosed in writing to Syros, you are not bound by the terms of any agreement with any previous employer or other party to refrain from using or disclosing any trade secret or confidential or proprietary information in the course of your employment with Syros, to refrain from competing, directly or indirectly, with the business of such previous employer or any other party or to refrain from soliciting employees, customers or suppliers of such previous employer or other party. You further represent that your performance of all the terms of this Agreement and the performance of your duties as an employee of Syros do not and will not conflict with or breach any agreement with any prior employer or other party to which you is a party (including without limitation any nondisclosure or non-competition agreement), and that you will not disclose to Syros or induce Syros to use any confidential or proprietary information or material belonging to any previous employer or others.

6. **United States Government Obligations**. You acknowledge that Syros from time to time may have agreements with other persons or with the United States Government, or agencies thereof, that impose obligations or restrictions on Syros regarding inventions made during the course of work under such agreements or regarding the confidential nature of such work. You agree to be bound by all such obligations and restrictions that are made known to you and to take all action necessary to discharge the obligations of Syros under such agreements.

7. **Miscellaneous**.

(a) **Equitable Remedies.** The restrictions contained in this Agreement are necessary for the protection of the business and goodwill of Syros and are considered by you to be reasonable for such purpose. You agree that any breach of this Agreement is likely to cause Syros substantial and irrevocable damage that is difficult to measure. Therefore, in the event of any such breach or threatened breach, you agree that Syros, in addition to such other remedies that may be available, shall have the right to obtain an injunction from a court restraining such a breach or threatened breach and the right to specific performance of the provisions of this Agreement, without any requirement of bond, and you hereby waive the adequacy of a remedy at law as a defense to such relief.

(b) **Obligations to Third Parties.** You acknowledge and represent that this agreement and your employment with Syros will not violate any continuing obligation you have to any former employer or other third party.

(c) **Disclosure of this Agreement.** You hereby agree to disclose this Agreement to any future employers or potential employers prior to commencing any formal work relationship with such employers or potential employers, and authorize Syros to notify others, including but not limited to customers of Syros and any of your future employers or prospective employers or business associates, of the terms and existence of this Agreement and your continuing obligations to Syros hereunder.

(d) **Not Employment Contract.** You acknowledge that this Agreement does not constitute a contract of employment, does not imply that Syros will continue your employment for any period of time, and does not change the at-will nature of your employment.

(e) **Successors and Assigns.** This Agreement shall be binding upon and inure to the benefit of both parties and their respective successors and assigns, including any corporation with which, or into which, Syros may be merged or which may succeed to Syros' assets or business; *provided, however,* that your obligations are personal and may not be assigned by you. You expressly consent to be bound by the provisions of this Agreement for the benefit of Syros or any subsidiary or affiliate thereof to whose employ you may be transferred without the necessity that this Agreement be re-signed at the time of such transfer.

(f) **Severability.** In case any provision of this Agreement shall be invalid, illegal or otherwise unenforceable, the validity, legality and enforceability of the remaining provisions shall in no way be affected or impaired thereby.

(g) **Waivers.** No delay or omission by Syros in exercising any right under this Agreement will operate as a waiver of that or any other right. A waiver or consent given by Syros on any one occasion is effective only in that instance and will not be construed as a bar to or waiver of any right on any other occasion.

(h) **Governing Law.** This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts (without reference to the conflicts of law provisions thereof). Any action, suit, or other legal proceeding which is commenced to resolve any matter arising under or relating to any provision of this Agreement shall be commenced only in a state or federal court located in the Commonwealth of Massachusetts and Syros and you each consent to the jurisdiction of such court. Syros and you each hereby irrevocably waive any right to a trial by jury in any action, suit or other legal proceeding arising under or relating to any provision of this Agreement. If Syros prevails in any action, suit or other legal proceeding to enforce this Agreement, you will reimburse Syros for all costs, including reasonable attorney's fees, it incurs in connection therewith.

(i) **Entire Agreement; Amendment.** This Agreement supersedes all prior agreements, written or oral, between you and Syros relating to the subject matter of this Agreement. This Agreement may not be modified, changed or discharged in whole or in part, except by an agreement in writing signed by you and Syros. You agree that any change or changes in your duties, title, salary or compensation after the signing of this Agreement shall not affect the validity or scope of this Agreement.

(j) **Captions.** The captions of the sections of this Agreement are for convenience of reference only and in no way define, limit or affect the scope or substance of any section of this Agreement.

YOU HAVE THE RIGHT TO CONSULT WITH LEGAL COUNSEL PRIOR TO SIGNING THIS AGREEMENT. YOU ACKNOWLEDGE THAT YOU HAVE CAREFULLY READ THIS AGREEMENT AND UNDERSTAND AND AGREE TO ALL OF ITS PROVISIONS.

WITNESS our hands and seals:

Date: 10 September 2021

SYROS PHARMACEUTICALS, INC.

By: /s/ Gerald Quirk
Gerald Quirk
Chief Operations Officer

Date: Sept 12, 2021

EMPLOYEE

/s/ Conley Chee
Name: Conley Chee

**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: November 5, 2021

**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, Jason Haas, 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/ Jason Haas

Jason Haas
Chief Financial Officer
(Principal Financial Officer)

Dated: November 5, 2021

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

In connection with the Quarterly Report on Form 10-Q of Syros Pharmaceuticals, Inc. (the "Company") for the quarter ended September 30, 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: November 5, 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.

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

In connection with the Quarterly Report on Form 10-Q of Syros Pharmaceuticals, Inc. (the "Company") for the quarter ended September 30, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Jason Haas, 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: November 5, 2021

/s/ Jason Haas

Jason Haas
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.