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, 2022

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	**45-3772460**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
35 CambridgePark Drive, 4th Floor Cambridge, Massachusetts	**02140**
(Address of Principal Executive Offices)	**(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 November 10, 2022: 20,225,921

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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;

•our planned clinical trials for our product candidates, whether conducted by us or by any 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;

•our ability to successfully integrate Tyme Therapeutics, Inc., or Tyme, and realize the anticipated benefits of the acquisition of Tyme, which was completed in September 2022;

•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 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, cash equivalents and marketable securities and the period of time in which such capital will be sufficient to fund our planned operations; and
- our estimates regarding expenses, future revenue, capital requirements and need for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained in this Quarterly Report.

We have included important factors in the cautionary statements included in this Quarterly Report, particularly in the "Risk Factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make. 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 coronavirus or treat its impact. COVID-19 has and may continue to adversely impact our operations and workforce, including our discovery research, supply chain and clinical trial operations activities, which in turn could have an adverse impact on our business and financial results.

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

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

You should read this Quarterly Report completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

PART I – FINANCIAL INFORMATION

Item 1. Financial Statements (unaudited)

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

	September 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 171,532	$ 92,302
Marketable securities	72,949	38,067
Contract assets	1,771	2,979
Prepaid expenses and other current assets	6,053	3,237
Total current assets	252,305	136,585
Property and equipment, net	12,062	12,844
Marketable securities – noncurrent	—	13,038
Other long-term assets	3,667	2,941
Restricted cash	3,086	3,086
Right-of-use asset – operating lease	13,464	14,104
Right-of-use assets – financing leases	141	337
Total assets	$ 284,725	$ 182,935
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 13,017	$ 3,692
Accrued expenses	21,713	15,624
Deferred revenue	1,625	10,181
Financing lease obligations, current portion	137	291
Operating lease obligation, current portion	1,932	1,720
Total current liabilities	38,424	31,508
Financing lease obligations, net of current portion	3	65
Operating lease obligation, net of current portion	21,385	22,858
Warrant liability	55,228	3,029
Debt, net of debt discount, long term	40,514	40,257
Commitments and contingencies (See Note 9)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized at September 30, 2022 and December 31, 2021; 0 shares issued and outstanding at September 30, 2022 and December 31, 2021	—	—
Common stock, $0.001 par value; 70,000,000 and 20,000,000 shares authorized at September 30, 2022 and December 31, 2021, respectively; 20,225,352 and 6,202,404 shares issued and outstanding at September 30, 2022 and December 31, 2021, respectively	20	6
Additional paid-in capital	682,836	548,870
Accumulated other comprehensive loss	(226)	(79)
Accumulated deficit	(553,459)	(463,579)
Total stockholders' equity	129,171	85,218
Total liabilities and stockholders' equity	$ 284,725	$ 182,935

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,	
	2022	2021	2022	2021
Revenue	$ 3,891	$ 5,697	$ 15,634	$ 15,686
Operating expenses:				
Research and development	25,759	27,262	84,030	73,077
General and administrative	8,076	5,346	21,970	16,606
Transaction related expenses	9,510	—	9,510	—
Total operating expenses	43,345	32,608	115,510	89,683
Loss from operations	(39,454)	(26,911)	(99,876)	(73,997)
Interest income	392	32	539	56
Interest expense	(1,051)	(984)	(3,008)	(2,921)
Change in fair value of warrant liability	9,860	1,836	12,465	14,117
Net loss applicable to common stockholders	$ (30,253)	$ (26,027)	$ (89,880)	$ (62,745)
Net loss per share applicable to common stockholders - basic and diluted	$ (3.21)	$ (4.14)	$ (11.93)	$ (10.06)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	9,417,069	6,292,830	7,536,149	6,239,482

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,	
	2022	2021	2022	2021
Net loss	$ (30,253)	$ (26,027)	$ (89,880)	$ (62,745)
Other comprehensive gain (loss):				
Unrealized holding gain (loss) on marketable securities	87	14	(147)	(5)
Comprehensive loss	$ (30,166)	$ (26,013)	$ (90,027)	$ (62,750)

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, 2022 and 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 December 31, 2020	5,622,274	$ 5	$ 467,569	$ —	$ (377,021)	$ 90,553
Exercise of stock options	2,013	—	157	—	—	157
Vesting of restricted stock units	26,701	—	—	—	—	—
Issuance of shares under Employee Stock Purchase Plan	3,305	—	153	—	—	153
Stock-based compensation expense	—	—	7,479	—	—	7,479
Issuance of common stock at-the-market, net of issuance costs of $5,132	540,000	1	70,467	—	—	70,468
Other comprehensive loss	—	—	—	(5)	—	(5)
Net loss	—	—	—	—	(62,745)	(62,745)
Balance at September 30, 2021	6,194,293	$ 6	$ 545,825	$ (5)	$ (439,766)	$ 106,060
Balance at December 31, 2021	6,202,403	$ 6	$ 548,870	$ (79)	$ (463,579)	$ 85,218
Exercise of stock options	3,770	—	1	—	—	1
Vesting of restricted stock units	83,569	1	—	—	—	1
Issuance of shares under Employee Stock Purchase Plan	13,293	—	108	—	—	108
Stock-based compensation expense	—	—	8,507	—	—	8,507
Issuance of shares in private placement, net of issuance cost of $5,068	6,387,173	6	60,106	—	—	60,112
Issuance of shares in merger, net of issuance cost of $3,136	7,546,014	7	65,325	—	—	65,332
Redemption of fractional shares due to reverse stock split	(10,870)	—	(81)	—	—	(81)
Other comprehensive loss	—	—	—	(147)	—	(147)
Net loss	—	—	—	—	(89,880)	(89,880)
Balance at September 30, 2022	20,225,352	$ 20	$ 682,836	$ (226)	$ (553,459)	$ 129,171

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDER'S EQUITY
For the three months ended September 30, 2022 and 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, 2021	6,192,025	$ 6	$ 543,729	$ (19)	$ (413,739)	$ 129,977
Vesting of restricted stock units	2,268	—	—	—	—	—
Stock-based compensation expense	—	—	2,096	—	—	2,096
Other comprehensive gain	—	—	—	14	—	14
Net loss	—	—	—	—	(26,027)	(26,027)
Balance at September 30, 2021	6,194,293	$ 6	$ 545,825	$ (5)	$ (439,766)	$ 106,060
Balance at June 30, 2022	6,298,898	$ 7	$ 554,531	$ (313)	$ (523,206)	$ 31,019
Vesting of restricted stock units	4,137	—	—	—	—	—
Stock-based compensation expense	—	—	2,955	—	—	2,955
Issuance of shares in private placement, net of issuance cost of $5,068	6,387,173	6	60,106	—	—	60,112
Issuance of shares in merger, net of issuance cost of $3,136	7,546,014	7	65,325	—	—	65,332
Redemption of fractional shares due to reverse stock split	(10,870)	—	(81)	—	—	(81)
Other comprehensive gain	—	—	—	87	—	87
Net loss	—	—	—	—	(30,253)	(30,253)
Balance at September 30, 2022	20,225,352	$ 20	$ 682,836	$ (226)	$ (553,459)	$ 129,171

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

	Nine Months Ended September 30,	
	2022	**2021**
Operating activities		
Net loss	$ (89,880)	$ (62,745)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	2,001	2,050
Amortization of right-of-use asset	196	195
Transaction related expenses allocated to warrants issued in connection with private placement	5,015	—
Stock-based compensation expense	8,507	7,479
Change in fair value of warrant liability	(12,465)	(14,117)
Net amortization of premiums and discounts on marketable securities	198	122
Amortization of debt-discount and accretion of deferred debt costs	557	521
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(1,466)	(1,813)
Accounts receivable	—	7
Contract assets	1,208	(1,308)
Other long-term assets	(726)	(694)
Accounts payable	323	334
Accrued expenses	3,727	1,048
Deferred revenue	(8,556)	(7,111)
Operating lease asset and liabilities	(621)	(539)
Net cash used in operating activities	(91,982)	(76,571)
Investing activities		
Purchases of property and equipment	(567)	(1,000)
Purchases of marketable securities	—	(51,408)
Maturities of marketable securities	30,031	—
Net cash (used in) provided by investing activities	29,464	(52,408)
Financing activities		
Payments on financing and capital lease obligations	(216)	(196)
Proceeds from issuance of common stock through employee benefit plans	—	157
Proceeds from the issuance of common stock through employee stock purchase plan	109	153
Proceeds from the issuance of common stock through exercise of option	1	—
Cash and cash equivalents acquired in connection with merger, net of issuance costs paid	14,166	—
Payment to creditor related to debt modification	(300)	—
Proceeds from issuance of common stock and accompanying warrants and pre-funded warrants in private placement, net of issuance costs	128,093	—
Proceeds from issuance of common stock and warrants in public offering, net of issuance costs	—	70,337
Redemption of fractional shares due to the reverse stock split	(81)	—
Payment of issuance cost related to out of period offering	(24)	(36)
Net cash (used in) provided by financing activities	141,748	70,415
Net (decrease) increase in cash, cash equivalents and restricted cash	79,230	(58,564)
Cash, cash equivalents and restricted cash (See reconciliation in Note 6)		
Beginning of period	95,388	177,070
End of period	$ 174,618	$ 118,506
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 2,417	$ 2,380
Non-cash investing and financing activities:		
Property and equipment received but unpaid as of period end	$ 678	$ 178
Offering costs incurred but unpaid as of period end	$ 10,746	$ 10

See accompanying notes to unaudited condensed consolidated financial statements.

1. Nature of Business

Syros Pharmaceuticals, Inc. (the "Company"), a Delaware corporation formed in November 2011, is a biopharmaceutical company seeking to redefine the power of small molecules to control the expression of genes.

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

The Company has incurred significant 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 $86.6 million, $84.0 million and $75.4 million for the years ended December 31, 2021, 2020 and 2019, respectively. As of September 30, 2022, the Company had an accumulated deficit of $553.5 million. The Company has not generated any revenues from product sales, has not completed the development of any product candidate and may never have a product candidate approved for commercialization. The Company has financed its operations to date primarily through a credit facility, the sale of equity securities and through license and collaboration agreements. 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.

On September 16, 2022, the Company filed an amendment to its Restated Certificate of Incorporation (the "Restated Certificate of Incorporation") with the Secretary of State of the State of Delaware to effect the reverse stock split of its common stock, such that every 10 shares of the Company's common stock held by a stockholder immediately prior to the reverse stock split were combined and reclassified into one share of the Company's common stock (the "Reverse Stock Split"). Except where otherwise indicated, all share and per share amounts in the accompanying financial statements, related footnotes, and management's discussion and analysis have been adjusted retroactively to reflect the Reverse Stock Split as if it had occurred at the beginning of the earliest period presented.

On September 16, 2022, the Company completed its acquisition of Tyme Technologies, Inc., a Delaware corporation ("Tyme"), in accordance with an Agreement and Plan of Merger, dated as of July 3, 2022 (the "Merger Agreement"). The Company issued approximately 7.5 million shares of its common stock to the former Tyme stockholders in exchange for all of the shares of Tyme common stock issued and outstanding immediately prior to the merger, with Tyme surviving as a wholly-owned subsidiary of the Company (the "Merger"). In connection with the closing of the Merger, and in accordance with the terms of the Merger Agreement, the Company acquired net cash, cash equivalents and marketable securities of approximately $67.1 million.

On September 16, 2022, the Company issued in a private placement (the "2022 Private Placement") 6,387,173 shares of common stock, and, in lieu of shares of common stock, pre-funded warrants (the "2022 Pre-Funded Warrants") to purchase an aggregate of up to 7,426,739 shares of common stock, and, in each case, accompanying warrants (the "2022 Warrants") to purchase an aggregate of up to 13,813,912 additional shares of common stock (or 2022 Pre-Funded Warrants to purchase common stock in lieu thereof) at a price of $10.34 per share and accompanying 2022 Warrant (or $10.33 per 2022 Pre-Funded Warrant and accompanying 2022 Warrant). The 2022 Private Placement resulted in aggregate gross proceeds of $129.9 million, before $10.1 million of transaction costs.

Based on its current operating plan, the Company's management believes that its cash, cash equivalents and marketable securities of $244.5 million as of September 30, 2022 will allow the Company to meet its liquidity requirements for a period of at least 12 months from the issuance date of this Quarterly Report on Form 10-Q.

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").

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, 2022, the results of its operations for the three and nine months ended September 30, 2022 and 2021, statements of stockholders' equity for the three and nine months ended September 30, 2022 and 2021, and statements of cash flows for the nine months ended September 30 2022 and 2021. Such adjustments are of a normal and recurring nature. The results for the three and nine months ended September 30, 2022 are not necessarily indicative of the results for the year ending December 31, 2022, or for any future period.

Principles of Consolidation

The accompanying condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, (i) 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, (ii) Syros Pharmaceuticals (Ireland) Limited, an Irish limited liability company formed by the Company in January 2019, and (iii) Tyme Technologies, Inc., a Delaware corporation, which is the surviving corporation in connection with the filing of a certificate of merger with the Secretary of State of the State of Delaware on September 16, 2022, pursuant to which Tack Acquisition Corp., a Delaware corporation formed by the Company in June 2022 to effect the Merger, merged with and into Tyme Technologies, Inc. (refer to Note 1). 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, income taxes and the evaluation of the existence of conditions and events that raise substantial doubt regarding the Company's ability to continue as a going concern. Actual results may differ from those estimates or assumptions.

Segment Information

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

Cash and Cash Equivalents

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

Off-Balance Sheet Risk and Concentrations of Credit Risk

The Company has no financial instruments with off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially subject the Company to concentrations of credit risk primarily consist of cash equivalents and marketable securities. Under its investment policy, the Company limits amounts invested in such securities by credit rating, maturity, industry group, investment type and

issuer, except for securities issued by the U.S. government. The Company is not exposed to any significant concentrations of credit risk from these financial instruments. The goals of the Company's investment policy, in order of priority, are safety and preservation of principal and liquidity of investments sufficient to meet cash flow requirements.

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.

Property and Equipment

Property and equipment consists of laboratory equipment, computer equipment, furniture and fixtures and leasehold improvements, all of which are stated at cost, less accumulated depreciation. Expenditures for maintenance and repairs that do not improve or extend the lives of the respective assets are recorded to expense as incurred. Major betterments are capitalized as additions to property and equipment. Depreciation and amortization are recognized over the estimated useful lives of the assets using the straight-line method.

Construction-in-progress is stated at cost, which relates to the cost of leasehold improvements not yet placed into service. No depreciation expense is recorded on construction-in-progress until such time as the relevant assets are completed and put into use.

Impairment of Long-Lived Assets

The Company continually evaluates long-lived assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book values of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book values of the assets exceed their fair value. The Company has not recognized any impairment losses from inception through September 30, 2022.

Other Long-Term Assets

Other long-term assets primarily consisted of advance payments made to the contract research organizations responsible for conducting the Company's tamibarotene and SY-5609 clinical trials.

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 non-refundable 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 non-refundable 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 awards.

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.

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.

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, 2022, 100,000 pre-funded warrants to purchase common stock issued in connection with the December 2020 private placement (the "2020 Pre-Funded Warrants"), and 7,426,749 2022 Pre-Funded Warrants issued in connection with the September 2022 private placement (refer to Note 11) 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,	
	2022	**2021**
Stock options	1,547,190	626,435
Unvested restricted stock units	521,316	185,096
Warrants*	14,354,007	499,010
Total	16,422,513	1,310,541

* As of September 30, 2022 , this is comprised of 211,709 warrants to purchase common stock issued in connection with the Company's April 2019 financing (refer to Note 11), 2,754 warrants to purchase common stock issued in connection with the execution of the Company's loan agreement in February 2020 (refer to Note 8), 1,738 warrants to purchase common stock issued in connection with the second draw on this loan agreement in December 2020 (refer to Note 8), 282,809 warrants to purchase common stock issued in connection with the private placement in December 2020 (refer to Note 11), 13,813,912 warrants to purchase common stock issued in connection with the private placement in September 2022 (refer to Note 11), and 41,085 warrants to purchase Syros common stock that were issued upon the assumption and conversion of Tyme warrants in connection with the Merger (refer to Note 3). As of September 30, 2021, this is comprised of 211,709 warrants to purchase common stock issued in connection with the Company's April 2019 financing (refer to Note 11), 2,754 warrants to purchase common stock issued in connection with the execution of the Company's loan agreement in February 2020 (refer to Note 8), 1,738 warrants to purchase common stock issued in connection with the second draw on this loan

agreement in December 2020 (refer to Note 8), and 282,809 warrants to purchase common stock issued in connection with the private placement in December 2020 (refer to Note 11).

Recent Accounting Pronouncements

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"), which requires the measurement and recognition of expected credit losses for financial assets held at amortized cost. ASU 2016-13 replaces the existing incurred loss impairment model with an expected loss model that requires the use of forward-looking information to calculate credit loss estimates. It also eliminates the concept of other-than-temporary impairment and requires credit losses on available-for-sale debt securities to be recorded through an allowance for credit losses instead of as a reduction in the amortized cost basis of the securities. As a smaller reporting company, ASU 2016-13 will become effective for the Company for fiscal years beginning after December 15, 2022, and 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.

Recently Adopted 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. The Company has adopted on a modified retrospective basis the new standard effective January 1, 2022, and it did not have a material impact on its condensed consolidated financial statements and related disclosures.

3. Recapitalization

On September 16, 2022, the Company issued approximately 7.5 million shares of its common stock to the former Tyme stockholders in connection with the Merger. The Company also issued options and warrants to purchase 733,545 shares of the Company's common stock to certain holders of Tyme options and warrants that were outstanding immediately before the consummation of the Merger. The Merger is accounted for as a recapitalization because the Company was determined to be a legal and accounting acquirer under Financial Accounting Standards Board's Accounting Standards Codification Topic 805, Business Combinations ("ASC 805"). This determination was primarily based on the following facts and circumstances:

- The pre-combination equity holders of the Company hold the relative majority of voting rights in the combined entity;
- The pre-combination equity holders of the Company have the right to appoint the majority of the directors on the combined entity's board of directors;
- Senior management of the Company comprises the senior management of the combined entity;
- Operations of the Company comprise the ongoing operations of the combined entity; and
- Upon effectiveness of the Merger, the primary assets of Tyme at the effective date were primarily cash, cash equivalents and marketable securities.

Under the recapitalization accounting model, the net assets acquired are recognized at fair value and any excess consideration transferred over the fair value of the net assets are reflected as a reduction to equity. Transaction costs incurred attributable to the Merger are also reflected as a reduction to the equity.

The carrying value of Tyme's net assets as of September 16, 2022, which approximates fair value because of its short-term nature, is set forth below:

	Fair Value
Cash and cash equivalents	$ 14,898
Marketable securities	52,220
Prepaid expenses	1,350
Total	$ 68,468

No value has been ascribed to the development programs acquired from Tyme in the Merger.

The Company incurred $3.1 million of transaction costs attributable to the Merger which are reflected as a reduction of additional paid-in capital. In addition, the Company paid $4.5 million of severance to former Tyme employees which is included in the Company's statement of operations as transaction related expenses.

4. 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"), now a subsidiary of Pfizer Inc., 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 estimated 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. As of December 31, 2021, the Company reduced the transaction price from the initial estimate of $60.0 million to $54.2 million. During the nine months ended September 30, 2022, the Company further reduced the transaction price from $54.2 million to $49.3 million. The reductions in the transaction price were driven by changes in the amount of reimbursable costs incurred and expected to be incurred by the Company.

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, 2022, the Company recognized revenue of $3.7 million and $14.4 million, respectively, under the GBT Collaboration Agreement. 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. As of September 30, 2022, the Company had deferred revenue outstanding under the GBT Collaboration Agreement of approximately $1.6 million, all of which is classified as deferred revenue, current portion 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, 2022, 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, 2022, the Company recognized revenue of $0.2 million and $1.2 million, respectively, under the Incyte Collaboration Agreement. 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. As of September 30, 2022, the Company had deferred revenue outstanding under the Incyte Collaboration Agreement of approximately $40.0 thousand, all of which is classified as deferred revenue, current portion 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, 2022 (in thousands):

	Balance at December 31, 2021	Additions	Deductions	Balance at September 30, 2022
Accounts receivable and contract assets:				
Billed receivables from collaboration partners	$ —	$ 8,288	$ (8,288)	$ —
Unbilled receivables from collaboration partners	2,979	7,476	(8,684)	1,771
Total accounts receivable and contract assets	$ 2,979	$ 15,764	$ (16,972)	$ 1,771
Contract liabilities:				
Deferred revenue - Incyte	$ 1,268	$ —	$ (1,228)	$ 40
Deferred revenue - GBT	8,913	199	(7,527)	1,585
Total contract liabilities	$ 10,181	$ 199	$ (8,755)	$ 1,625

5. 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, 2022 and December 31, 2021 (in thousands):

September 30, 2022	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash and money market funds	$ 170,122	$ —	$ —	$ 170,122
Commercial paper	1,410	—	—	1,410
Marketable securities:				
Corporate debt securities - due in one year or less	29,823	1	(138)	29,686
Commercial paper	12,145	—	—	12,145
Municipal bonds	19,208	8	—	19,216
US Treasury obligation - due in one year or less	12,000	—	(98)	11,902
Total	$ 244,708	$ 9	$ (236)	$ 244,481

December 31, 2021	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash and money market funds	$ 92,302	$ —	$ —	$ 92,302
Marketable securities:				
Corporate debt securities - due in one year or less	30,100	—	(12)	30,088
US Treasury obligation - due in one year or less	8,000	—	(21)	7,979
Corporate debt securities - due in more than one year to five years	9,085	—	(33)	9,052
US Treasury obligation - due in more than one year to five years	3,999	—	(13)	3,986
Total	$ 143,486	$ —	$ (79)	$ 143,407

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, 2022 and 2021, 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, 2022, 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, 2022, the Company held 50 securities that were in an unrealized loss position. The aggregate fair value of securities held by the Company in an unrealized loss position for less than 12 months as of September 30, 2022 was $33.1 million. There were seven securities held by the Company in an unrealized loss position for more than 12 months as of September 30, 2022. 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, 2022.

6. Fair Value Measurements

Assets and liabilities measured at fair value on a recurring basis as of September 30, 2022 and December 31, 2021 were as follows (in thousands):

Description	September 30, 2022	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Cash	$ 165,984	$ 165,984	—	$ —
Money market funds	4,138	4,138	—	—
Commercial paper	1,410	—	1,410	—
Corporate debt securities - due in one year or less	29,686	—	29,686	—
Commercial paper	12,145	—	12,145	—
Municipal bonds	19,216	—	19,216	—
US Treasury obligation - due in one year or less	11,902	11,902	—	—
Total	$ 244,481	$ 182,024	$ 62,457	$ —
Liabilities:				
Warrant liability	$ 55,228	$ —	$ —	$ 55,228
Total	$ 55,228	$ —	$ —	$ 55,228

Description	December 31, 2021	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Cash	$ 57,213	$ 57,213	$ —	$ —
Money market funds	35,089	35,089	—	—
Corporate debt securities - due in one year or less	30,088	—	30,088	—
US Treasury obligation - due in one year or less	7,979	7,979	—	—
US Treasury obligation - due in more than one year to five years	3,986	3,986	—	—
Corporate debt securities - due in more than one year to five years	9,052	—	9,052	—
Total	$ 143,407	$ 104,267	$ 39,140	$ —
Liabilities:				
Warrant liability	$ 3,029	$ —	$ —	$ 3,029
Total	$ 3,029	$ —	$ —	$ 3,029

Assumptions Used in Determining Fair Value of Warrants

The Company issued the 2022 Warrants to purchase an aggregate of up to 13,813,912 shares of common stock in connection with the 2022 Private Placement (see Note 11) and warrants to purchase an aggregate of up to 282,809 shares of common stock in connection with a private placement on December 8, 2020 (the "2020 Warrants") (see Note 11). The Company accounted for the 2022 Warrants and 2020 Warrants as liabilities. The Company recorded the fair value of these warrants upon issuance using the Black-Scholes valuation model and is required to revalue these 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, 2022	September 16, 2022	December 31, 2021
Stock price	$ 6.44	$ 7.35	$ 3.26
Risk-free interest rate	4.07 %	3.62 %	1.11 %
Dividend yield	—	—	—
Expected life (in years)	4.92	5.00	3.94
Expected volatility	86.76 %	86.10 %	81.14 %

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, 2022 and the year ended December 31, 2021 (in thousands):

	September 30, 2022	December 31, 2021
Fair value of warrant liability as of beginning of the period	$ 3,029	$ 19,711
Fair value of 2022 Warrants issued in connection with private placement	64,664	—
Change in fair value	(12,465)	(16,682)
Fair value of warrant liability as of end of the period	$ 55,228	$ 3,029

7. Restricted Cash

At September 30, 2022 and December 31, 2021, the Company had $3.1 million in restricted cash, which was classified as long-term on the Company's condensed consolidated balance sheets, and all of which was attributable to the HQ Lease (See Note 9).

In connection with the execution of the HQ 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 HQ 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, 2022, December 31, 2021 (in thousands):

	September 30, 2022	December 31, 2021
Cash and cash equivalents	$ 171,532	$ 92,302
Restricted cash, net of current portion	3,086	3,086
Total cash, cash equivalents and restricted cash	$ 174,618	$ 95,388

8. 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"). Pursuant to the terms of an amendment to the Loan Agreement dated July 3, 2022 (the "Loan Agreement Amendment"), effective September 16, 2022, Oxford agreed to extend the interest-only period from March 1, 2023 to March 1, 2024 and to extend the Maturity Date from February 1, 2025 to February 1, 2026, and (iii) upon the achievement of certain milestones and subject to the payment of certain fees, further extend the interest only period to September 1, 2024 and the Maturity Date to August 1, 2026.

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 also paid fees of $300,000 related to the Loan Agreement Amendment. 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, 2022 (in thousands):

Three months ending December 31, 2022	$	—
Year ending December 31, 2023		—
Year ending December 31, 2024		15,000
Year ending December 31, 2025		20,000
Year ending December 31, 2026		5,000
Total minimum payments	$	40,000
Less unamortized debt discount		(612)
Plus accumulated accretion of final fees		1,126
Total carrying value of debt		40,514
Less current portion		—
Long-term debt, net of current portion	$	40,514

For the three and nine months ended September 30, 2022, interest expense related to the Loan Agreement was approximately $1.0 million and $3.0 million, respectively. 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. The long-term portion of debt is $40.5 million as classified on the Company's condensed consolidated balance sheets as of September 30, 2022.

9. Accrued Expenses

Accrued expenses consisted of the following as of September 30, 2022 and December 31, 2021 (in thousands):

	September 30, 2022	December 31, 2021
External research and preclinical development	$ 11,450	$ 8,274
Employee compensation and benefits	6,747	6,344
Professional fees	3,377	953
Facilities and other	139	53
Accrued expenses	$ 21,713	$ 15,624

10. Commitments and Contingencies

Operating Lease

On January 8, 2019, the Company entered into a lease (the "HQ 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 HQ Lease has escalating rent payments and the Company records rent expense on a straight-line basis over the term of the HQ Lease, including any rent-free periods.

In connection with the execution of the HQ 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 HQ 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 HQ Lease starting at the lease commencement date on a straight-line basis. On the Company's condensed consolidated balance sheets, the Company classified $1.9 million of the lease liability as short-term and $21.4 million of the lease liability as long-term as of September 30, 2022.

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 HQ 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, 2022 (in thousands):

	Operating	Financing
Three months ending December 31, 2022	$ 998	$ 78
Year ending December 31, 2023	4,049	66
Year ending December 31, 2024	4,166	—
Year ending December 31, 2025	4,287	—
Year ending December 31, 2026 and beyond	19,256	—
Total minimum lease payments	32,756	144
Less imputed interest	(9,439)	(4)
Total lease liability	$ 23,317	$ 140

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, 2022 (in thousands):

	Three Months Ended September 30, 2022	Nine Months Ended September 30, 2022
Lease cost:		
Operating lease cost	$ 772	$ 2,316
Financing lease cost:		
Amortization of right-of-use asset	$ 65	$ 196
Interest on lease liabilities	4	18
Total financing lease cost	$ 69	$ 214
Cash paid for amounts included in the measurement of liabilities:		
Operating cash flows from operating lease		$ 2,937
Operating cash flows from financing lease		$ 234

Other information:	Nine Months Ended September 30, 2022
Weighted-average remaining lease term (in years) - operating lease	7.42
Weighted-average discount rate - operating lease	9.30 %
Weighted-average remaining lease term (in years) - financing lease	0.89
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 is required to pay to Orsenix:

- an upfront fee of $12.0 million, which was paid with cash on hand upon the closing of the transaction;
- single-digit million milestone payments related to the development of SY-2101 in indications other than 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 Agreement

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 incurred no fees under this supply management agreement during the three months ended September 30, 2022, and incurred fees of $1.8 million during the nine months ended September 30, 2022, respectively. The Company incurred fees of $0.6 million and $0.8 million under this supply management agreement during the three and nine months ended September 30, 2021, respectively.

11. Stockholders' Equity

Increase of Authorized Shares and Reverse Stock Split

Effective on September 15, 2022. the number of authorized shares of the Company's common stock was increased from 200,000,000 shares (on a pre-split basis) to 700,000,000 shares (on a pre-split basis).

On September 16, 2022, the number of authorized shares of the Company's common stock was proportionately adjusted from 700,000,000 to 70,000,000 as a result of the Reverse Stock Split. Immediately following the Reverse Stock Split, and without giving effect to the shares of the Company's common stock issued in connection with the Merger and the 2022 Private Placement, there were approximately 6.3 million shares of the Company's common stock outstanding. The Company's common stock began trading on The Nasdaq Global Select Market on a split-adjusted basis on September 19, 2022.

No fractional shares were issued in connection with the Reverse Stock Split. Any fractional shares resulting from the Reverse Stock Split were rounded down to the nearest whole number, and each stockholder who would have otherwise been entitled to a fraction of a share of common stock upon the Reverse Stock Split (after aggregating all fractions of a share to which such stockholder would have otherwise been entitled) was, in lieu thereof, entitled to receive a cash payment.

Issuance of Securities through a Private Placement

On September 16, 2022, the Company issued in a private placement 6,387,173 shares of common stock, and, in lieu of shares of common stock, the 2022 Pre-Funded Warrants to purchase an aggregate of 7,426,739 shares of common stock, and, in each case, the accompanying 2022 Warrants to purchase an aggregate of up to 13,813,912 additional shares of common stock (or 2022 Pre-Funded Warrants to purchase common stock in lieu thereof) at a price of $10.34 per share and accompanying 2022 Warrant (or $10.33 per 2022 Pre-Funded Warrant and accompanying 2022 Warrant).

The 2022 private placement resulted in aggregate gross proceeds of $129.9 million, before $10.1 million of transaction costs.

On December 8, 2020, the Company issued in a private placement 1,031,250 shares of common stock, and, in lieu of shares of common stock, the 2020 Pre-Funded Warrants to purchase an aggregate of 100,000 shares of common stock, and, in each case, the accompanying 2020 Warrants to purchase an aggregate of up to 282,809 additional shares of common stock (or 2020 Pre-Funded Warrants to purchase common stock in lieu thereof) at a price of $80.00 per share and accompanying 2020 Warrant (or $79.90 per 2020 Pre-Funded Warrant and accompanying 2020 Warrant). The 2020 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 the 2022 Warrants and 2020 Warrants may require the Company to make a payment based on a Black-Scholes valuation, using specified inputs. The holders of 2022 Pre-Funded Warrants and 2020 Pre-Funded Warrants do not have similar rights. Therefore, the Company accounted for the 2022 Warrants and 2020 Warrants as liabilities, while the 2022 Pre-Funded Warrants and 2020 Pre-Funded Warrants met the permanent equity criteria classification. The 2022 Pre-Funded Warrants and 2020 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 2022 Pre-Funded Warrants and 2020 Pre-Funded Warrants do not provide any guarantee of value or return. The initial fair value of the 2022 Warrants and the 2020 Warrants at issuance was $64.7 million and $19.3 million, respectively, determined using the Black-Scholes valuation model. The Company remeasured the aggregate fair value of the 2022 Warrants and the 2020 Warrants at September 30, 2022 and December 31, 2021 as $55.2 million and $3.0 million, respectively. The change in fair value of $9.9 million and $12.5 million was recorded in the condensed statement of operations for the three and nine months ended September 30, 2022, respectively.

Issuance of Securities through an Underwritten Public Offering

On January 22, 2021, the Company issued and sold an aggregate of 540,000 shares of its common stock in an underwritten public offering at a public offering price of $140.00 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.

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 866,733 shares of its common stock and accompanying Class A warrants (the "2019 Warrants") to purchase 195,184 shares of the Company's common stock at a combined price to the public of $75.0 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 16,650 shares of the Company's common stock at a combined public offering price of $75,000 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 66,600 shares of common stock. As of September 30, 2022, there were no shares of Series A Preferred Stock outstanding.

Each 2019 Warrant has an exercise price per share of common stock of $86.25, 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.

As of September 30, 2022, the 2019 Warrants to purchase 211,709 shares of common stock are outstanding and remain unexercised.

12. 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. Under the 2016 Plan, stock options may not be granted at less than fair value on the date of grant. The 2016 Plan was replaced by 2022 Equity Incentive Plan on September 16, 2022, and no further awards may be made under the 2016 Plan.

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) 117,333 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, 2022, the number of shares reserved for issuance under the 2016 ESPP was increased by 62,024 shares. At September 30, 2022, 272,436 shares remained available for future issuance under the 2016 ESPP.

Inducement Grants

During the year ended December 31, 2021, the Company granted non-statutory stock options to purchase an aggregate of 111,000 shares of the Company's common stock. These stock options were granted outside of the 2016 Plan as an inducement material to the applicable employee's acceptance of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).These stock options will vest over a four-year period, with 25% of the shares underlying each 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 each option is subject to such employee's continued service with the Company through the applicable vesting dates.

2022 Inducement Stock Incentive Plan

On January 25, 2022, the Company's board of directors adopted the 2022 Inducement Stock Incentive Plan (the "2022 Plan"), pursuant to which the Company may grant non-statutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards with respect to an aggregate of 100,000 shares of common stock. Awards under the 2022 Plan may only be granted to persons who (i) were not previously an employee or director of the Company or (ii) are commencing employment with the Company following a bona fide period of non-employment, in either case as an inducement material to the individual's entering into employment with the Company and in accordance with the requirements of Nasdaq Stock Market Rule 5635(c)(4). At September 30, 2022, 59,580 shares remained available for future issuance under the 2022 Plan.

2022 Equity Incentive Plan

The 2022 Stock Incentive Plan (the "2022 EIP") was adopted by the board of directors on July 14, 2022, approved by the stockholders and became effective on September 15, 2022. The 2022 EIP replaced the 2016 Plan. Any options or awards outstanding under the 2016 Plan remained outstanding and effective. Under the 2022 EIP, the Company may grant incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards. 4,737,534 shares of the Company's common stock are reserved for issuance under the 2022 EIP. At September 30, 2022, 2,962,863 shares remained available for future issuance under the 2022 EIP. Under the 2022 EIP, stock options may not be granted at less than fair value on the date of grant.

Stock Options

Terms of stock option agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the applicable stock 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.

A summary of the status of stock options as of December 31, 2021 and September 30, 2022 and changes during the nine months ended September 30, 2022 is presented below:

	Shares	Weighted Average Exercise Price	Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2021	665,727	$ 82.70	7.2	$ 4,936
Granted	911,336	30.94		
Exercised	(3,770)	0.40		
Cancelled	(26,103)	87.80		
Outstanding at September 30, 2022	1,547,190	$ 51.76	4.5	$ —
Exercisable at September 30, 2022	1,179,506	$ 56.28	2.9	$ —

Pursuant to the terms of the Merger Agreement, the Company assumed certain Tyme stock options that were outstanding and unexercised immediately prior to the completion of the Merger. The Company issued options to purchase 692,460 shares of the Company's common stock at the completion of the Merger on September 16, 2022. The original terms and restrictions on such Tyme options shall continue in full force and effect except for certain options held by certain Tyme employees which were modified to extend the exercise period to up to two years. The Company recorded $0.4 million of one-time additional stock-based compensation expense related to the modification.

The intrinsic value of stock options exercised during the nine months ended September 30, 2022 and 2021 was $0.1 million and $0.1 million, respectively.

As of September 30, 2022, there was $9.5 million of total unrecognized compensation cost related to unvested stock options granted to employees, which is expected to be recognized over a weighted-average period of 2.8 years.

Restricted Stock Units and Restricted Stock Awards

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. In addition, pursuant to our director compensation policy, members of our board of directors have been granted, at their election, either restricted stock units or restricted stock awards, which awards vest annually over a three-year term with 33.33% vesting on each anniversary of the grant date. The fair value of restricted stock units and restricted stock awards are 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 and restricted stock awards as of December 31, 2021 and September 30, 2022 and changes during the nine months ended September 30, 2022 is presented below:

	Shares Subject to Restricted Stock Units and Restricted Stock Awards	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2021	268,749	$ 65.21
Granted	383,523	14.41
Vested	(83,622)	72.97
Forfeited	(47,334)	55.15
Outstanding at September 30, 2022	521,316	$ 28.83

As of September 30, 2022, there was $10.8 million of unrecognized stock-based compensation expense related to outstanding restricted stock units and restricted stock awards, with an expected recognition period of 2.5 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,	
	2022	2021	2022	2021
Weighted-average risk-free interest rate	3.60 %	1.12 %	2.85 %	0.87 %
Expected dividend yield	— %	— %	— %	— %
Expected option term (in years)	5.79	6.06	5.88	6.01
Volatility	83.27 %	81.24 %	82.18 %	81.88 %

The weighted-average grant date fair value per share of options granted in the nine months ended September 30, 2022 and 2021 was $7.82 and $6.36, 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,	
	2022	2021	2022	2021
Research and development	$ 1,496	$ 1,485	$ 4,324	$ 4,260
General and administrative	1,459	611	4,183	3,219
Total stock-based compensation expense	$ 2,955	$ 2,096	$ 8,507	$ 7,479

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, 2021 that we filed with the Securities and Exchange Commission, or SEC, on March 15, 2022, or the 2021 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 2021 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 clinical-stage product candidates are:

•tamibarotene, a selective retinoic acid receptor alpha, or RARα, 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 to enable the conduct of a Phase 3 clinical trial in patients with newly diagnosed acute promyelocytic leukemia, or APL; and

•SY-5609, a highly selective and potent oral inhibitor of cyclin-dependent kinase 7, or CDK7, that we are evaluating in combination with chemotherapy in pancreatic cancer patients in an expansion cohort of our existing Phase 1 clinical trial, which is being evaluated in combination with atezolizumab, a PD-L1 inhibitor, in BRAF-mutant colorectal cancer in an arm of a Phase 1/1b clinical trial sponsored by F. Hoffmann-La Roche AG, or Roche, which is now actively enrolling.

We also have multiple preclinical and discovery programs in oncology, including programs targeting the inhibition of CDK12, CDK11, and WRN. In July 2022, we advanced our oral, potent, and selective CDK12 inhibitor, SY-12882, to development candidate. Preclinical data presented at the American Association for Cancer Research (AACR) annual meeting in April 2022 demonstrated that selective CDK12 inhibition resulted in strong anti-tumor activity as a single agent and in combination with a DNA damaging agent and in combination with a poly adenosine diphosphate-ribose polymerase, or PARP, inhibitor in models of breast, lung, and ovarian cancer. We are seeking partnerships for our oncology discovery programs, including CDK12.

In December 2019, we entered into a collaboration with Global Blood Therapeutics, Inc., now a subsidiary of Pfizer 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.

Tamibarotene

At the 62nd American Society of Hematology Annual Meeting and Exposition held in December 2020, or ASH 2020, we presented 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 RARα, biomarker. As of an October 1, 2020 data cut-off, 51 newly diagnosed unfit AML patients, including patients with and without *RARA* gene overexpression, 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 patients with *RARA* overexpression 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 patients without *RARA* overexpression 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 translational data demonstrating that most newly diagnosed unfit AML patients with *RARA* overexpression enrolled in our Phase 2 study had 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 25,000 patients are diagnosed with unfit AML in the United States and Europe annually and we expect the overall total addressable market opportunity for all AML patients to grow to approximately $6.6 billion by 2025.

Based on these data and our assessment of ongoing areas of high unmet need, we advanced tamibarotene in combination with azacitidine into a registration-enabling Phase 3 clinical trial in newly diagnosed HR-MDS patients with *RARA* overexpression, which we refer to as SELECT-MDS-1. HR-MDS is a hematologic malignancy that is closely related to AML, and we believe that approximately 50% of HR-MDS patients overexpress *RARA*. We believe that approximately 21,000 patients are diagnosed with HR-MDS in the United States and Europe annually and we expect the total addressable market opportunity for MDS patients of all risk groups to grow to approximately $3.3 billion by 2026. We plan to enroll approximately 190 newly diagnosed HR-MDS patients with *RARA* overexpression 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 we expect to report data from the SELECT-MDS-1 trial in the fourth quarter of 2023 or first quarter of 2024, with a potential submission to the U.S. Food and Drug Administration, or FDA, of a new drug application, or NDA, expected in 2024.

In addition, we are advancing tamibarotene in combination with venetoclax and azacitidine in newly diagnosed unfit AML patients with *RARA* overexpression. The trial, which we refer to as SELECT-AML-1, is designed with a single-arm safety lead-in of approximately 15 patients 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 strategy for patients in the control arm who do not respond to venetoclax and azacitidine. We have begun dosing patients in the SELECT AML-1 trial and expect to report clinical activity data from the safety lead-in portion of the ongoing trial at the 64th Annual Meeting of the American Society of Hematology on Saturday, December 10, 2022. We expect to report data from the randomized portion of the trial in 2023 or 2024.

In March 2022, we entered into an agreement with QIAGEN Manchester Limited, or QIAGEN, under which QIAGEN agreed to develop and commercialize an assay as a companion diagnostic test to determine the expression level of our proprietary *RARA* biomarker for use with tamibarotene in newly diagnosed higher-risk MDS patients. QIAGEN will also be responsible for obtaining and maintaining regulatory approvals for the commercial diagnostic test.

SY-2101

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. APL represents approximately 10% of all AML cases, and approximately 2,000 patients are diagnosed with APL in the United States and Europe annually. 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 low-risk 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. If SY-2101 demonstrates comparable efficacy to IV ATO in our clinical studies, we believe it has the potential to become the standard-of-care frontline therapy for APL by providing 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 ongoing dose confirmation study is evaluating the PK, food effect, safety and tolerability of SY-2101 and is expected to enroll between six and 24 adult APL patients undergoing consolidation with IV ATO plus ATRA. Participants receive a single dose of 15 mg of SY-2101 in both the fasted and in the fed state, and a single dose of IV ATO for PK assessments, with flexibility to allow for other SY-2101 doses to be evaluated. Daily administration of SY-2101 is also being evaluated in a multiple-dose treatment module substituting for IV ATO during consolidation to assess steady state SY-2101 PK and safety. Based on preliminary data available to date, SY-2101 administered at 15 mg achieved comparable PK (AUC and Cmax) exposures to IV ATO at the approved dose of 0.15 mg/kg. Additionally, based on the data available to date, SY-2101 showed high oral bioavailability of approximately 80% and continues to support a favorable tolerability profile.

The feedback from a Type C meeting to review our Phase 3 study design with the FDA in November 2021 continues to support molecular complete response rate as the primary endpoint for accelerated approval and event free survival as the primary endpoint for full approval, in each case compared to historic IV ATO data. FDA feedback supports the inclusion of patients randomized to IV ATO for comparative safety assessments. In addition, feedback received in July 2022 from the European Medicines Agency, or EMA, on the Phase 3 study design also indicated that our proposed Phase 3 clinical trial could support regulatory approval in the European Union. Based on this feedback and 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 approximately 215 patients with newly diagnosed APL, randomized 2:1 to receive SY-2101 or IV ATO, in the second half of 2023.

SY-5609

At the European Society for Medical Oncology Congress held in September 2021, or ESMO 2021, we presented data from the ongoing 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, or 7d on/7d off, and five days on treatment and two days off, or 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 gastrointestinal (nausea, diarrhea, decreased appetite, abdominal pain, vomiting), fatigue, thrombocytopenia, and anemia. Tolerability was optimized with the 7d on/7d off schedule, which had the lowest rates of treatment-emergent AEs relative to other regimens, 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 response-evaluable 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 SD 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 preclinical data at ESMO 2021 evaluating the anti-tumor and PD activity of intermittent dosing regimens for SY-5609, as well as preclinical data evaluating SY-5609 as a single agent and in combination with chemotherapy in pancreatic cancer models.

Based on these data, we are enrolling patients in an expansion cohort that includes two arms evaluating SY-5609 in combination with chemotherapy for the treatment of pancreatic cancer, one of which is evaluating SY-5609 in combination with gemcitabine in patients in first or second relapse who have progressed following treatment with the chemotherapy regimen known as FOLFIRINOX, and the other is exploring SY-5609 in combination with gemcitabine and nab-paclitaxel in patients following first relapse after FOLFIRINOX. SY-5609 is administered 7d on/7d off at a starting dose of 4 mg in both the gemcitabine combination and triplet combination arms, and the combination agents will be administered at the approved doses. The study is designed to evaluate safety and tolerability, as well as efficacy measures such as progression free survival and disease control rate, or DCR, which is the combined rate of CR, partial response, or PR, and SD.

As of a October 12, 2022 safety data cut-off, a maximum tolerated dose, or MTD, of single agent SY-5609 administered in a 7 day on/7 day off dosing regimen has not been reached. The 10 mg dose level did not result in any dose limiting toxicities, or DLTs, further supporting the tolerability of the 7 day on/7 day off dosing regimen in which 30 patients have been dosed across five dose levels (4, 5, 6, 7, and 10 mg), with one DLT observed at the 4 mg single agent dose level. PK analyses demonstrated an expected increase in SY-5609 exposure levels, with the 10 mg single-agent dose also supporting a preliminary exposure-response relationship. At the time of the October 20, 2022 clinical activity data-cut off, two of three study patients treated at the 10 mg dose level were response evaluable, with two of two response-evaluable patients achieving SD (one with pancreatic ductal adenocarcinoma, or PDAC, and one with colorectal cancer, or CRC), with the PDAC patient experiencing a 10% tumor reduction. As of the safety data cut-off, an MTD for either the doublet or the triplet has not been reached in the 7 day on/7 day off dosing regimen, with dosing of SY-5609 up to 5 mg in the doublet and up to 4 mg in the triplet regimen, respectively. SY-5609 has been safely combined with gemcitabine and with gemcitabine plus nab-paclitaxel, with no new safety signals identified and the majority of AEs being low grade and reversible. The most common related AEs in the cohort with SY-5609 and gemcitabine, where the highest SY-5609 doses were evaluated in combination with chemotherapy, included fatigue, nausea, decreased appetite and decreased platelet count (all low grade), with one patient experiencing a DLT of grade 3 diarrhea at the 5 mg SY-5609 dose level. No DLTs were reported in patients treated with SY-5609 in combination with gemcitabine/nab-paclitaxel. As of the clinical activity data cut-off, initial doublet activity of SY-5609 plus gemcitabine in PDAC included a confirmed PR by Response Evaluation Criteria in Solid Tumors, or RECIST, accompanied by a 98% reduction in the CA 19-9 tumor marker from a baseline of 60,357 U/mL to 968 U/mL, in one of four response evaluable patients treated at the 4 mg SY-5609 dose level, corresponding to a 25% DCR, and SD in three of four response evaluable patients treated at the 5 mg SY-5609 dose level, corresponding to a 75% DCR, for an overall DCR of 50% (four out of eight) in response evaluable patients. There is preliminary evidence for an exposure-response relationship, with the responding patient who achieved a confirmed PR demonstrating higher-than-average exposure relative to other patients at that dose. Two of three patients treated at the 4 mg dose level in the triplet regimen cohort were response evaluable, including one with SD. We intend to continue dose escalation in the single agent cohort for select solid tumors to a dose of 15mg and in the doublet combination cohort in PDAC patients to a dose of 10 mg of SY-5609 plus gemcitabine. In parallel, we plan to seek a partnership for the further development of SY-5609.

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 is being evaluated in combination with atezolizumab in patients with BRAF-mutant disease, and this arm of the trial is now actively enrolling. 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.

Strategic Financing

On July 3, 2022, we entered into an Agreement and Plan of Merger, or the Merger Agreement, with Tack Acquisition Corp., a Delaware corporation and a wholly-owned subsidiary of us, or the Merger Sub, and Tyme Technologies, Inc., a Delaware corporation, or Tyme, providing for the merger of the Merger Sub with and into Tyme, with Tyme surviving the merger as our wholly-owned subsidiary, or the Merger. In connection with the closing of the Merger on September 16, 2022, and in accordance with the terms of the Merger Agreement, we acquired net cash, cash equivalents and marketable securities of approximately $62.6 million.

Also on July 3, 2022, immediately prior to the execution and delivery of the Merger Agreement, we entered into a Securities Purchase Agreement with certain accredited investors, pursuant to which the investors agreed to purchase shares of our common stock and/or pre-funded warrants to purchase shares of our common stock, and accompanying warrants to purchase additional shares of our common stock (or pre-funded warrants in lieu thereof), or the PIPE Financing.

On September 16, 2022, the PIPE Financing closed concurrently with the Merger. At the closing of the Merger, we issued an aggregate of 7,546,014 shares of our common stock to Tyme stockholders. In the PIPE Financing, we issued an aggregate of 6,387,173 shares of our common stock and, in lieu of shares to certain investors, pre-funded warrants to purchase an aggregate of 7,426,739 shares of common stock, and, in each case, accompanying warrants to purchase an aggregate of up to 13,813,912 additional shares of common stock (or pre-funded warrants to purchase common stock in lieu thereof). We received aggregate gross proceeds from the PIPE Financing of $130 million, before deducting estimated offering expenses payable by us not inclusive of any exercise of the warrants.

Financial Operations Overview

Revenue

To date, 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, 2022 and 2021, we recognized $3.9 million and $5.7 million of revenue, respectively, of which $3.7 million and $5.6 million was related to our collaboration with GBT and $0.2 million and $0.1 million to our collaboration with Incyte, respectively. For the nine months ended September 30, 2022 and 2021, we recognized $15.6 million and $15.7 million of revenue, respectively, of which $14.4 million and $12.9 million was related to our collaboration with GBT and $1.2 million and $2.8 million to our collaboration with Incyte, respectively.

Expenses

Research and Development Expenses

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

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

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

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

The following table summarizes our external research and development expenses by program, as well as expenses not allocated to programs, for the three and nine months ended September 30, 2022 and 2021 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Tamibarotene external costs	$ 9,363	$ 8,464	$ 31,310	$ 22,028
SY-5609 and other CDK7 program external costs	1,233	2,650	5,290	8,576
SY-2101 program external costs	498	1,277	3,227	3,035
Other research and platform program external costs	3,654	5,564	11,505	12,797
Employee-related expenses, including stock-based compensation	9,174	7,515	27,133	21,596
Facilities and other expenses	1,837	1,792	5,565	5,045
Total research and development expenses	$ 25,759	$ 27,262	$ 84,030	$ 73,077

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 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 investigational new drug applications, or INDs, 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 continuing 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.

Transaction Related Expenses

Transaction related expenses primarily consist of incurred costs allocated to the warrants issued in connection with the PIPE Financing that were accounted for as liabilities, and severance paid to former Tyme employees.

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 2021 10-K.

Results of Operations

Comparison of three months ended September 30, 2022 and 2021

The following table summarizes our results of operations for the three months ended September 30, 2022 and 2021, together with the changes in those items in dollars (in thousands):

	Three Months Ended September 30, 2022	2021	Dollar Change	% Change
Statements of Operations Data:				
Revenue	$ 3,891	$ 5,697	$ (1,806)	(32) %
Operating expenses:				
Research and development	25,759	27,262	(1,503)	(6) %
General and administrative	8,076	5,346	2,730	51 %
Transaction related expenses	9,510	—	9,510	— %
Total operating expenses	43,345	32,608	10,737	33 %
Loss from operations	(39,454)	(26,911)	(12,543)	47 %
Interest income	392	32	360	1,125 %
Interest expense	(1,051)	(984)	(67)	7 %
Change in fair value of warrant liability	9,860	1,836	8,024	437 %
Net loss	$ (30,253)	$ (26,027)	$ (4,226)	16 %

Revenue

For the three months ended September 30, 2022, revenue was $3.9 million, of which $3.7 million was attributable to our collaboration with GBT and $0.2 million was attributable to our collaboration with Incyte. 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.

Research and Development Expense

Research and development expense decreased by approximately $1.5 million, or 6%, from $27.3 million for the three months ended September 30, 2021 to $25.8 million for the three months ended September 30, 2022. The following table summarizes our research and development expenses for the three months ended September 30, 2022 and 2021, together with the changes to those items in dollars (in thousands):

	Three Months Ended September 30, 2022	2021	Dollar Change	% Change
External research and development	$ 12,796	$ 15,907	$ (3,111)	(20) %
Employee-related expenses, excluding stock-based compensation	7,678	6,030	1,648	27 %
Stock-based compensation	1,496	1,485	11	1 %
Consulting, licensing and professional fees	1,952	2,048	(96)	(5) %
Facilities and other expenses	1,837	1,792	45	3 %
Total research and development expenses	$ 25,759	$ 27,262	$ (1,503)	(6) %

The decrease in research and development expense was primarily attributable to the decrease in clinical trials' start-up costs and activities associated with our preclinical programs, including the following:

- a decrease of approximately $3.1 million, or 20%, for external research and development costs, primarily due to a decrease in costs related to our preclinical programs;

- an increase of approximately $1.6 million, or 27%, for employee-related expenses, including increased salary and benefits, primarily due to our increased headcount; and

•a decrease of approximately $0.1 million, or 5%, for consulting, licensing and professional fees, primarily related to decreases in costs associated with our pre-clinical programs and SY-5609.

General and Administrative Expense

General and administrative expense increased by approximately $2.8 million, or 51%, from $5.3 million for the three months ended September 30, 2021 to $8.1 million for the three months ended September 30, 2022. The change in general and administrative expense was primarily attributable to an increase in employee-related expenses, and an increase in recruiting fees.

Transaction Related Expenses

Transaction related expenses primarily consist of incurred costs allocated to the warrants issued in connection with the PIPE Financing that were accounted for as liabilities, and severance paid to former Tyme employees.

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, 2022 as compared to the three months ended September 30, 2021 was due to the higher interest rate during the three month period ended September 30, 2022 compared to the same period in 2021.

Interest Expense

Interest expense was related to our credit facility with Oxford and equipment financing arrangements. Interest expense increased slightly from the three months ended September 30, 2021 to the three months ended September 30, 2022 due to a higher average outstanding credit facility balance during the three month period ended September 30 2022.

Change in Fair Value of Warrant Liability

The change in fair value of warrant liability during the three months ended September 30, 2022 as compared to the three months ended September 30, 2021 was a result of the remeasurement of the fair value of warrants issued in connection with the September 2022 and December 2020 private placements.

Comparison of nine months ended September 30, 2022 and 2021

The following table summarizes our results of operations for the nine months ended September 30, 2022 and 2021, together with the changes in those items in dollars (in thousands):

	Nine Months Ended September 30, 2022	2021	Dollar Change	% Change
Statements of Operations Data:				
Revenue	$ 15,634	$ 15,686	$ (52)	(0) %
Operating expenses:				
Research and development	84,030	73,077	10,953	15 %
General and administrative	21,970	16,606	5,364	32 %
Transaction related expenses	9,510	—	9,510	— %
Total operating expenses	115,510	89,683	25,827	29 %
Loss from operations	(99,876)	(73,997)	(25,879)	35 %
Interest income	539	56	483	863 %
Interest expense	(3,008)	(2,921)	(87)	3 %
Change in fair value of warrant liability	12,465	14,117	(1,652)	(12) %
Net loss	$ (89,880)	$ (62,745)	$ (27,135)	43 %

Revenue

For the nine months ended September 30, 2022, revenue was $15.6 million, of which $14.4 million was attributable to our collaboration with GBT and $1.2 million was attributable to our collaboration with Incyte. 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.

Research and Development Expense

Research and development expense increased by approximately $11.0 million, or 15%, from $73.1 million for the nine months ended September 30, 2021 to $84.0 million for the nine months ended September 30, 2022. The following table summarizes our research and development expenses for the nine months ended September 30, 2022 and 2021, together with the changes to those items in dollars (in thousands):

	Nine Months Ended September 30, 2022	2021	Dollar Change	% Change
External research and development	$ 46,678	$ 41,726	$ 4,952	12 %
Employee-related expenses, excluding stock-based compensation	22,809	17,336	5,473	32 %
Stock-based compensation	4,324	4,260	64	2 %
Consulting, licensing and professional fees	4,654	4,710	(56)	(1) %
Facilities and other expenses	5,565	5,045	520	10 %
Total research and development expenses	$ 84,030	$ 73,077	$ 10,953	15 %

The increase 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 $5.0 million, or 12%, for external research and development costs, primarily due to an increase in costs associated with the continued advancement of our clinical trials of tamibarotene, offset by a decrease in costs associated with our preclinical programs;

- an increase of approximately $5.5 million, or 32%, for employee-related expenses, including increased salary and benefits, primarily due to our increased headcount; and

- an increase of approximately $0.5 million, or 10%, for facilities and other expenses, primarily due to our increased headcount.

General and Administrative Expense

General and administrative expense increased by approximately $5.4 million, or 32%, from $16.6 million for the nine months ended September 30, 2021 to $22.0 million for the nine months ended September 30, 2022. The change in general and administrative expense was primarily attributable to an increase in employee-related expenses, recruiting fees, and software costs.

Transaction Related Expenses

Transaction related expenses primarily consist of incurred costs allocated to the warrants issued in connection with the PIPE Financing that were accounted for as liabilities, and severance paid to former Tyme employees.

Interest Income

Interest income was derived generally from our investments in cash, cash equivalents and marketable securities. The increase in interest income during the nine months ended September 30, 2022 as compared to the nine months ended September 30, 2021 was due to a higher interest rate in marketable securities during the nine months ended September 30, 2022 compared to the same period in 2021.

Interest Expense

Interest expense was related to our credit facility with Oxford and equipment financing arrangements. Interest expense for the nine months ended September 30, 2022 has slightly increased compared to the interest expense for the

nine months ended September 30, 2021 due to higher average outstanding credit facility balance during the nine months ended September 30, 2022.

Change in Fair Value of Warrant Liability

The change in fair value of warrant liability during the nine months ended September 30, 2022 as compared to the nine months ended September 30, 2021 was a result of the remeasurement of the fair value of warrants issued in connection with the September 2022 and December 2020 private placements.

Liquidity and Capital Resources

Sources of Liquidity

We funded our operations from inception through September 30, 2022, 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 July 3, 2022, we entered into the Merger Agreement with Tyme. Also on July 3, 2022, immediately prior to the execution and delivery of the Merger Agreement, we entered into the Securities Purchase Agreement with certain accredited investors.

In connection with the closing of the Merger on September 16, 2022, and in accordance with the terms of the Merger Agreement, we acquired net cash, cash equivalents and marketable securities of approximately $67.1 million. The PIPE Financing closed concurrently with the Merger on September 16, 2022, pursuant to which we received aggregate gross proceeds of $129.9 million, before deducting offering expenses payable by us, and not inclusive of any exercise of the warrants issued in the PIPE Financing.

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. On July 3, 2022, we entered into an amendment, or the Loan Amendment, to the Loan Agreement with Oxford. Pursuant to the Loan Amendment, Oxford has agreed to modify the Loan Agreement in order to, among other things, extend the interest only period from March 1, 2023 to March 1, 2024 and extend the maturity date from February 1, 2025 to February 1, 2026, and (iii) upon the achievement of certain milestones and subject to the payment of certain fees, further extend the interest only period to September 1, 2024 and maturity date to August 1, 2026. As of September 30, 2022, $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, 2022, $75.0 million in common stock remained available for future issuance under the sales agreement.

As of September 30, 2022, $224.4 million of securities remained available for future issuance under the shelf registration statement.

As of September 30, 2022, we had cash, cash equivalents and marketable securities of approximately $244.5 million.

Cash Flows

The following table provides information regarding our cash flows for the nine months ended September 30, 2022 and 2021 (in thousands):

	Nine Months Ended September 30, 2022	2021
Net cash provided by (used in):		
Operating activities	$ (91,982)	$ (76,571)
Investing activities	29,464	(52,408)
Financing activities	141,748	70,415
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 79,230	$ (58,564)

Net Cash Used in Operating Activities

Net cash used in operating activities for the nine months ended September 30, 2022 and 2021 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 $92.0 million during the nine months ended September 30, 2022 compared to $76.6 million for the nine months ended September 30, 2021. The increase in net cash used in operating activities during the nine months ended September 30, 2022 was primarily due to an increase of $27.1 million loss from operations offset by a $5.0 million transaction cost allocated to warrants issued in connection with the PIPE Financing and a $4.0 million change in the net operating assets balances during the nine months ended September 30, 2022.

Net Cash Provided by (Used in) Investing Activities

Net cash provided by investing activities was $29.5 million during the nine months ended September 30, 2022 compared to net cash used in investing activities of $52.4 million during the nine months ended September 30, 2021. The net cash provided by investing activities was primarily due to the maturity of marketable securities of $30.0 million, offset by the purchase of $0.5 million of property and equipment during the nine months ended September 30, 2022. The net cash used in investing activities was due to the $1.0 million purchase of property and equipment and the $51.4 million investments in marketable securities during the nine months ended September 30, 2021.

Net Cash Provided by Financing Activities and Merger

Net cash provided by financing activities was $141.8 million during the nine months ended September 30, 2022 compared to $70.4 million for the nine months ended September 30, 2021. Cash provided by financing activities for the nine months ended September 30, 2022 was primarily due to $128.1 million of proceeds from the issuance of common stock and accompanying 2022 Warrants and 2022 Pre-Funded Warrants in the PIPE Financing, net of issuance costs and $14.2 million of proceeds from the Merger (recapitalization), net of issuance costs, partially offset by the payment of $0.3 million to Oxford related to an amendment to our Loan and Security Agreement, and $0.2 million of payments made under our financing lease. In comparison, the 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 financing lease.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue to advance our clinical trials of tamibarotene, SY-2101 and SY-5609, 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, 2022, will enable us to fund our planned operating expense and capital expenditure requirements into 2025. 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 clinical pipeline 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 continuing 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, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

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

Item 3. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments, including cash equivalents, are in the form of money market funds and marketable securities and are invested in U.S. treasury or government obligations. However, because of the short-term nature of the duration of our portfolio and the low-risk profile of our investments, we believe an immediate 10% change in market interest rates would not be expected to have a material impact on the fair market value of our 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, 2022, 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, 2022 and 2021.

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, 2022, 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, 2021, or the 2021 10-K. Any of the risk factors contained in this Quarterly Report on Form 10-Q and the 2021 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 Our Financial Position and Need for Additional Capital

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

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time consuming, expensive and uncertain process. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We believe that our cash, cash equivalents and marketable securities as of September 30, 2022 will enable us to fund our planned operating expense and capital expenditure requirements into 2025. Our estimate as to how long we expect our existing cash, cash equivalents and marketable securities to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. In any event, our existing cash, cash equivalents and marketable securities will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of our product candidates or our other preclinical programs.

Our future funding requirements will depend on many factors, including those discussed in Part I, Item 1A, "Risk Factors" in the 2021 10-K under "*Risks Related to Our Financial Position and Need for Additional Capital - We have incurred significant losses since inception, expect to incur significant and increasing losses for at least the next several years, and may never achieve or maintain profitability*." Our future funding requirements may also depend on:

- whether a drug candidate will be nominated to enter into 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 costs of precommercial activities related to our product candidates, including 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, LLC, associated with the development and commercialization of SY-2101; and

- the timing and amount of milestone payments due to QIAGEN Manchester Limited associated with the development and commercialization of a companion diagnostic test for use with tamibarotene.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We expect our expenses to remain high in connection with our planned operations. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, as we did through a public offering of our common stock in January 2021, the ownership interests of our existing stockholders may be substantially diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect our stockholders' rights. In addition, debt financing, such as our term loan facility with Oxford that we entered into in February 2020 and amended in July 2022, has created fixed payment obligations and imposed restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise additional funds through collaborations or marketing, distribution or licensing arrangements with third parties, such as our collaboration agreement with GBT, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds 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. In this regard, we recently announced that we are seeking a partnership for the clinical development of SY-5609 as we continue dose escalation, and that we are seeking partnerships for our oncology discovery programs, including our CDK12 program. However, we cannot provide assurance that these transactions will be consummated, or that sufficient additional capital to support the further development of SY-5609 following dose escalation or of our oncology discovery programs can be obtained or will be obtained on favorable terms.

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

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial resources, we intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. In this regard, we announced in November 2022 that we have elected to seek a partnership for the further development of SY-5609 as we continue dose escalation.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

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 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 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 unfit AML or patient subsets within newly diagnosed unfit 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 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 IV ATO 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 ATO 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 ATO compound for the treatment of autoimmune diseases. We are also aware of an oral formulation of ATO being studied in an academic setting in Hong Kong.

In addition, we are aware of selective CDK7 inhibitors being developed in early clinical trials by Carrick Therapeutics Ltd., Exelixis, Inc. and Qurient Co. Ltd., as well as other selective CDK7 inhibitor programs that we believe are in preclinical development from Yungjin Pharma Co., Ltd., The Translational Genomics Research Institute, Applied Pharmaceutical Science, Inc. and Kirilys Therapeutics, Inc., and a collaboration between Exscientia Ltd. and GT Apeiron Therapeutics Ltd. focused on developing novel cyclin-dependent kinase, or 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 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 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 collaborators, are able to obtain approval for ours, which could result in our competitors establishing a strong market position before we, or any collaborators, are able to enter the market.

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

Risks Related to the Merger

We may be unable to integrate Tyme successfully and realize the anticipated benefits of the merger.

Prior to the completion of the Merger, Syros and Tyme operated independently. We may fail to realize some or all of the anticipated benefits of the Merger if the integration process takes longer than expected or is more costly than expected. It is possible that the integration process could result in the diversion of our management's attention, the disruption or interruption of, or the loss of momentum in, our ongoing business or inconsistencies in standards, controls, procedures and policies, any of which could adversely affect our ability to maintain relationships with third parties or the ability to achieve the anticipated benefits of the Merger, or could otherwise adversely affect our business and financial results.

We may be exposed to increased litigation, including stockholder litigation, which could have an adverse effect on our business and operations.

We may be exposed to increased litigation from stockholders, customers, suppliers, consumers and other third parties due to the combination of our business and Tyme's business following the Merger. Such litigation may have an adverse

impact on our business and results of operations or may cause disruptions to our operations. In addition, in the past, stockholders have initiated class action lawsuits against biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources, which could have a material adverse effect our business, financial condition and results of operations.

Item 6. Exhibits.

Exhibit No.	Description of Exhibit
2.1*	Agreement and Plan of Merger, dated July 3, 2022, by and among the Registrant, Tack Acquisition Corp. and Tyme Technologies, Inc. (incorporated by reference to Exhibit 2.1 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on July 5, 2022).
3.1	Restated Certificate of Incorporation of the Registrant, including the Certificate of Designation of Preferences, Rights and Limitation of Series A Convertible Preferred Stock of the Registrant, as amended (filed herewith).
3.2	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).
4.1	Form of Warrant to Purchase Common Stock or Pre-Funded Warrants (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on July 5, 2022).
4.2	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on July 5, 2022).
10.1	Form of Syros Support Agreement (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on July 5, 2022).
10.2	Form of Tyme Support Agreement (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on July 5, 2022).
10.3	Form of Lock-up Agreement (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on July 5, 2022).
10.4	Securities Purchase Agreement, dated July 3, 2022, by and among the Registrant and the persons party thereto (incorporated by reference to Exhibit 10.4 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on July 5, 2022).
10.5	Registration Rights Agreement, dated July 3, 2022, by and among the Registrant and the persons party thereto (incorporated by reference to Exhibit 10.5 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on July 5, 2022).
10.6	Registration Rights Agreement, dated July 3, 2022, by and among the Registrant, 667, L.P. and Baker Brothers Life Sciences, L.P. (incorporated by reference to Exhibit 10.6 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on July 5, 2022).
10.7	Amendment to Loan and Security Agreement, dated July 3, 2022, by and among the Registrant and Oxford Finance LLC, as collateral agent and lender (incorporated by reference to Exhibit 10.7 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on July 5, 2022).
10.8	Second Amendment to Loan and Security Agreement, dated August 31, 2022, by and among the Registrant and Oxford Finance LLC, as collateral agent and lender (filed herewith).

10.9**	Syros Pharmaceuticals, Inc. 2022 Equity Incentive Plan (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on September 15, 2022).
10.10**	Form of Stock Option Agreement Under 2022 Equity Incentive Plan (filed herewith).
10.11**	Form of Restricted Stock Unit Agreement Under 2022 Equity Incentive Plan (filed herewith).
10.12**	Form of Restricted Stock Agreement Under 2022 Equity Incentive Plan (filed herewith).
10.13**	Syros Pharmaceuticals, Inc. Amended and Restated Director Compensation Policy (filed herewith).
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
32.1	Certification of principal executive officer pursuant to Rule 13a-14(b) promulgated under the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code.
32.2	Certification of principal financial officer pursuant to Rule 13a-14(b) promulgated under the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code.
101.INS	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document).
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Presentation Linkbase Document
104	Cover Page Interactive Data (formatted as Inline XBRL and contained in Exhibit 101)
*	Exhibits and/or schedules have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The Company hereby undertakes to furnish supplementally copies of any of the omitted exhibits and schedules upon request by the SEC; provided, however, that the Company may request confidential treatment pursuant to Rule 24b-2 of the Exchange Act for any exhibits or schedules so furnished. A list identifying the contents of all omitted exhibits and schedules can be found on page iii of Exhibit 2.1.
**	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.

Syros Pharmaceuticals, Inc.

Date: November 14, 2022

By: /s/ Jason Haas
Jason Haas
Chief Financial Officer (Principal Financial Officer)

Exhibit 3.1

RESTATED CERTIFICATE OF INCORPORATION

OF

SYROS PHARMACEUTICALS, INC.

(originally incorporated on November 9, 2011 under the name LS22, Inc.)

FIRST: The name of the Corporation is Syros Pharmaceuticals, Inc.

SECOND: The address of the Corporation's registered office in the State of Delaware is Corporation Trust Center, 1209 Orange Street, in the City of Wilmington, County of New Castle, 19801. The name of its registered agent at that address is The Corporation Trust Company.

THIRD: The nature of the business or purposes to be conducted or promoted by the Corporation is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law of the State of Delaware.

FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is 210,000,000 shares, consisting of (i) 200,000,000 shares of Common Stock, $0.001 par value per share ("Common Stock"), and (ii) 10,000,000 shares of Preferred Stock, $0.001 par value per share ("Preferred Stock").

The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A. COMMON STOCK.

1. General. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights of the holders of the Preferred Stock of any series as may be designated by the Board of Directors upon any issuance of the Preferred Stock of any series.

2. Voting. The holders of the Common Stock shall have voting rights at all meetings of stockholders, each such holder being entitled to one vote for each share thereof held by such holder; provided, however, that, except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment to this Certificate of Incorporation (which, as used herein, shall mean the certificate of incorporation of the Corporation, as amended from time to time, including the terms of any certificate of designations of any series of Preferred Stock) that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more other such series, to vote thereon pursuant to this Certificate of Incorporation. There shall be no cumulative voting.

The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a majority of the stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of the State of Delaware.

3. Dividends. Dividends may be declared and paid on the Common Stock from funds lawfully available therefor as and when determined by the Board of Directors and subject to any preferential dividend or other rights of any then outstanding Preferred Stock.

4. Liquidation. Upon the dissolution or liquidation of the Corporation, whether voluntary or involuntary, holders of Common Stock will be entitled to receive all assets of the Corporation available for distribution to its stockholders, subject to any preferential or other rights of any then outstanding Preferred Stock.

B. PREFERRED STOCK.

Preferred Stock may be issued from time to time in one or more series, each of such series to have such terms as stated or expressed herein and in the resolution or resolutions providing for the issue of such series adopted by the Board of Directors of the Corporation as hereinafter provided. Any shares of Preferred Stock which may be redeemed, purchased or acquired by the Corporation may be reissued except as otherwise provided by law.

Authority is hereby expressly granted to the Board of Directors from time to time to issue the Preferred Stock in one or more series, and in connection with the creation of any such series, by adopting a resolution or resolutions providing for the issuance of the shares thereof and by filing a certificate of designations relating thereto in accordance with the General Corporation Law of the State of Delaware, to determine and fix the number of shares of such series and such voting powers, full or limited, or no voting powers, and such designations, preferences and relative participating, optional or other special rights, and qualifications, limitations or restrictions thereof, including without limitation thereof, dividend rights, conversion rights, redemption privileges and liquidation preferences, as shall be stated and expressed in such resolutions, all to the full extent now or hereafter permitted by the General Corporation Law of the State of Delaware. Without limiting the generality of the foregoing, the resolutions providing for issuance of any series of Preferred Stock may provide that such series shall be superior or rank equally or be junior to any other series of Preferred Stock to the extent permitted by law.

The number of authorized shares of Preferred Stock may be increased or decreased (but not below the number of shares then outstanding) by the affirmative vote of the holders of a majority of the voting power of the capital stock of the Corporation entitled to vote thereon, voting as a single class, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of the State of Delaware.

FIFTH: Except as otherwise provided herein, the Corporation reserves the right to amend, alter, change or repeal any provision contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by statute and this Certificate of Incorporation, and all rights conferred upon stockholders herein are granted subject to this reservation.

SIXTH: In furtherance and not in limitation of the powers conferred upon it by the General Corporation Law of the State of Delaware, and subject to the terms of any series of Preferred Stock, the Board of Directors shall have the power to adopt, amend, alter or repeal the By-laws of the Corporation by the affirmative vote of a majority of the directors present at any regular or special meeting of the Board of Directors at which a quorum is present. The stockholders may not adopt, amend, alter or repeal the By-laws of the Corporation, or adopt any provision inconsistent therewith, unless such action is approved, in addition to any other vote required by this Certificate of Incorporation, by the affirmative vote of the holders of at least seventy-five percent (75%) of the votes that all the stockholders would be entitled to cast in any annual election of directors or class of directors. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article SIXTH.

SEVENTH: Except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty, no director of the Corporation shall be personally liable to the Corporation or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability. No amendment to or repeal of this provision shall apply to or have any effect on the liability or alleged liability of any director of the Corporation for or with respect to any acts or omissions of such director occurring prior to such amendment or repeal. If the General Corporation Law of the State of Delaware is amended to permit further elimination or limitation of the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law of the State of Delaware as so amended.

EIGHTH: The Corporation shall provide indemnification as follows:

1. Actions, Suits and Proceedings Other than by or in the Right of the Corporation. The Corporation shall indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the Corporation) by reason of the fact that he or she is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) (all such persons being referred to hereafter as an “Indemnitee”), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys’ fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974), and amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. The termination of any action, suit or proceeding by judgment, order,

settlement, conviction or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that Indemnitee did not act in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his or her conduct was unlawful.

2. Actions or Suits by or in the Right of the Corporation. The Corporation shall indemnify any Indemnitee who was or is a party to or threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the Corporation to procure a judgment in its favor by reason of the fact that Indemnitee is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, except that no indemnification shall be made under this Section 2 in respect of any claim, issue or matter as to which Indemnitee shall have been adjudged to be liable to the Corporation, unless, and only to the extent, that the Court of Chancery of Delaware or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of such liability but in view of all the circumstances of the case, Indemnitee is fairly and reasonably entitled to indemnity for such expenses (including attorneys' fees) which the Court of Chancery of Delaware or such other court shall deem proper.

3. Indemnification for Expenses of Successful Party. Notwithstanding any other provisions of this Article EIGHTH, to the extent that an Indemnitee has been successful, on the merits or otherwise, in defense of any action, suit or proceeding referred to in Sections 1 and 2 of this Article EIGHTH, or in defense of any claim, issue or matter therein, or on appeal from any such action, suit or proceeding, Indemnitee shall be indemnified against all expenses (including attorneys' fees) actually and reasonably incurred by or on behalf of Indemnitee in connection therewith. Without limiting the foregoing, if any action, suit or proceeding is disposed of, on the merits or otherwise (including a disposition without prejudice), without (i) the disposition being adverse to Indemnitee, (ii) an adjudication that Indemnitee was liable to the Corporation, (iii) a plea of guilty or nolo contendere by Indemnitee, (iv) an adjudication that Indemnitee did not act in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the Corporation, and (v) with respect to any criminal proceeding, an adjudication that Indemnitee had reasonable cause to believe his or her conduct was unlawful, Indemnitee shall be considered for the purposes hereof to have been wholly successful with respect thereto.

4. Notification and Defense of Claim. As a condition precedent to an Indemnitee's right to be indemnified, such Indemnitee must notify the Corporation in writing as soon as practicable of any action, suit, proceeding or investigation involving such Indemnitee for which indemnity will or could be sought. With respect to any action, suit, proceeding or investigation of which the Corporation is so notified, the Corporation will be entitled to participate therein at its own expense and/or to assume the defense thereof at its own expense, with legal counsel reasonably

acceptable to Indemnitee. After notice from the Corporation to Indemnitee of its election so to assume such defense, the Corporation shall not be liable to Indemnitee for any legal or other expenses subsequently incurred by Indemnitee in connection with such action, suit, proceeding or investigation, other than as provided below in this Section 4. Indemnitee shall have the right to employ his or her own counsel in connection with such action, suit, proceeding or investigation, but the fees and expenses of such counsel incurred after notice from the Corporation of its assumption of the defense thereof shall be at the expense of Indemnitee unless (i) the employment of counsel by Indemnitee has been authorized by the Corporation, (ii) counsel to Indemnitee shall have reasonably concluded that there may be a conflict of interest or position on any significant issue between the Corporation and Indemnitee in the conduct of the defense of such action, suit, proceeding or investigation or (iii) the Corporation shall not in fact have employed counsel to assume the defense of such action, suit, proceeding or investigation, in each of which cases the fees and expenses of counsel for Indemnitee shall be at the expense of the Corporation, except as otherwise expressly provided by this Article EIGHTH. The Corporation shall not be entitled, without the consent of Indemnitee, to assume the defense of any claim brought by or in the right of the Corporation or as to which counsel for Indemnitee shall have reasonably made the conclusion provided for in clause (ii) above. The Corporation shall not be required to indemnify Indemnitee under this Article EIGHTH for any amounts paid in settlement of any action, suit, proceeding or investigation effected without its written consent. The Corporation shall not settle any action, suit, proceeding or investigation in any manner which would impose any penalty or limitation on Indemnitee without Indemnitee's written consent. Neither the Corporation nor Indemnitee will unreasonably withhold or delay its consent to any proposed settlement.

5. Advance of Expenses. Subject to the provisions of Section 6 of this Article EIGHTH, in the event of any threatened or pending action, suit, proceeding or investigation of which the Corporation receives notice under this Article EIGHTH, any expenses (including attorneys' fees) incurred by or on behalf of Indemnitee in defending an action, suit, proceeding or investigation or any appeal therefrom shall be paid by the Corporation in advance of the final disposition of such matter; provided, however, that the payment of such expenses incurred by or on behalf of Indemnitee in advance of the final disposition of such matter shall be made only upon receipt of an undertaking by or on behalf of Indemnitee to repay all amounts so advanced in the event that it shall ultimately be determined by final judicial decision from which there is no further right to appeal that Indemnitee is not entitled to be indemnified by the Corporation as authorized in this Article EIGHTH; and provided further that no such advancement of expenses shall be made under this Article EIGHTH if it is determined (in the manner described in Section 6 of this Article EIGHTH) that (i) Indemnitee did not act in good faith and in a manner he or she reasonably believed to be in, or not opposed to, the best interests of the Corporation, or (ii) with respect to any criminal action or proceeding, Indemnitee had reasonable cause to believe his or her conduct was unlawful. Such undertaking shall be accepted without reference to the financial ability of Indemnitee to make such repayment.

6. Procedure for Indemnification and Advancement of Expenses. In order to obtain indemnification or advancement of expenses pursuant to Section 1, 2, 3 or 5 of this Article EIGHTH, an Indemnitee shall submit to the Corporation a written request. Any such advancement of expenses shall be made promptly, and in any event within 60 days after receipt by the Corporation of the written request of Indemnitee, unless (i) the Corporation has assumed

the defense pursuant to Section 4 of this Article EIGHTH (and none of the circumstances described in Section 4 of this Article EIGHTH that would nonetheless entitle the Indemnitee to indemnification for the fees and expenses of separate counsel have occurred) or (ii) the Corporation determines within such 60-day period that Indemnitee did not meet the applicable standard of conduct set forth in Section 1, 2 or 5 of this Article EIGHTH, as the case may be. Any such indemnification, unless ordered by a court, shall be made with respect to requests under Section 1 or 2 only as authorized in the specific case upon a determination by the Corporation that the indemnification of Indemnitee is proper because Indemnitee has met the applicable standard of conduct set forth in Section 1 or 2 of this Article EIGHTH, as the case may be. Such determination shall be made in each instance (a) by a majority vote of the directors of the Corporation consisting of persons who are not at that time parties to the action, suit or proceeding in question ("disinterested directors"), whether or not a quorum, (b) by a committee of disinterested directors designated by majority vote of disinterested directors, whether or not a quorum, (c) if there are no disinterested directors, or if the disinterested directors so direct, by independent legal counsel (who may, to the extent permitted by law, be regular legal counsel to the Corporation) in a written opinion, or (d) by the stockholders of the Corporation.

7. Remedies. The right to indemnification or advancement of expenses as granted by this Article EIGHTH shall be enforceable by Indemnitee in any court of competent jurisdiction. Neither the failure of the Corporation to have made a determination prior to the commencement of such action that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Corporation pursuant to Section 6 of this Article EIGHTH that Indemnitee has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct. In any suit brought by Indemnitee to enforce a right to indemnification, or brought by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the Corporation shall have the burden of proving that Indemnitee is not entitled to be indemnified, or to such advancement of expenses, under this Article EIGHTH. Indemnitee's expenses (including attorneys' fees) reasonably incurred in connection with successfully establishing Indemnitee's right to indemnification, in whole or in part, in any such proceeding shall also be indemnified by the Corporation. Notwithstanding the foregoing, in any suit brought by Indemnitee to enforce a right to indemnification hereunder it shall be a defense that the Indemnitee has not met any applicable standard for indemnification set forth in the General Corporation Law of the State of Delaware.

8. Limitations. Notwithstanding anything to the contrary in this Article EIGHTH, except as set forth in Section 7 of this Article EIGHTH, the Corporation shall not indemnify an Indemnitee pursuant to this Article EIGHTH in connection with a proceeding (or part thereof) initiated by such Indemnitee unless the initiation thereof was approved by the Board of Directors of the Corporation. Notwithstanding anything to the contrary in this Article EIGHTH, the Corporation shall not indemnify an Indemnitee to the extent such Indemnitee is reimbursed from the proceeds of insurance, and in the event the Corporation makes any indemnification payments to an Indemnitee and such Indemnitee is subsequently reimbursed from the proceeds of insurance, such Indemnitee shall promptly refund indemnification payments to the Corporation to the extent of such insurance reimbursement.

9. Subsequent Amendment. No amendment, termination or repeal of this Article EIGHTH or of the relevant provisions of the General Corporation Law of the State of Delaware or any other applicable laws shall adversely affect or diminish in any way the rights of any Indemnitee to indemnification under the provisions hereof with respect to any action, suit, proceeding or investigation arising out of or relating to any actions, transactions or facts occurring prior to the final adoption of such amendment, termination or repeal.

10. Other Rights. The indemnification and advancement of expenses provided by this Article EIGHTH shall not be deemed exclusive of any other rights to which an Indemnitee seeking indemnification or advancement of expenses may be entitled under any law (common or statutory), agreement or vote of stockholders or disinterested directors or otherwise, both as to action in Indemnitee's official capacity and as to action in any other capacity while holding office for the Corporation, and shall continue as to an Indemnitee who has ceased to be a director or officer, and shall inure to the benefit of the estate, heirs, executors and administrators of Indemnitee. Nothing contained in this Article EIGHTH shall be deemed to prohibit, and the Corporation is specifically authorized to enter into, agreements with officers and directors providing indemnification rights and procedures different from those set forth in this Article EIGHTH. In addition, the Corporation may, to the extent authorized from time to time by its Board of Directors, grant indemnification rights to other employees or agents of the Corporation or other persons serving the Corporation and such rights may be equivalent to, or greater or less than, those set forth in this Article EIGHTH.

11. Partial Indemnification. If an Indemnitee is entitled under any provision of this Article EIGHTH to indemnification by the Corporation for some or a portion of the expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) or amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with any action, suit, proceeding or investigation and any appeal therefrom but not, however, for the total amount thereof, the Corporation shall nevertheless indemnify Indemnitee for the portion of such expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) or amounts paid in settlement to which Indemnitee is entitled.

12. Insurance. The Corporation may purchase and maintain insurance, at its expense, to protect itself and any director, officer, employee or agent of the Corporation or another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) against any expense, liability or loss incurred by him or her in any such capacity, or arising out of his or her status as such, whether or not the Corporation would have the power to indemnify such person against such expense, liability or loss under the General Corporation Law of the State of Delaware.

13. Savings Clause. If this Article EIGHTH or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the Corporation shall nevertheless indemnify each Indemnitee as to any expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) and amounts paid in settlement in connection with any action, suit, proceeding or investigation, whether civil, criminal or administrative, including an action by or in the right of the Corporation, to the fullest extent permitted by any applicable portion of this Article EIGHTH that shall not have been invalidated and to the fullest extent permitted by applicable law.

14. Definitions. Terms used herein and defined in Section 145(h) and Section 145(i) of the General Corporation Law of the State of Delaware shall have the respective meanings assigned to such terms in such Section 145(h) and Section 145(i).

NINTH: This Article NINTH is inserted for the management of the business and for the conduct of the affairs of the Corporation.

1. General Powers. The business and affairs of the Corporation shall be managed by or under the direction of the Board of Directors.

2. Number of Directors; Election of Directors. Subject to the rights of holders of any series of Preferred Stock to elect directors, the number of directors of the Corporation shall be established by the Board of Directors. Election of directors need not be by written ballot, except as and to the extent provided in the By-laws of the Corporation.

3. Classes of Directors. Subject to the rights of holders of any series of Preferred Stock to elect directors, the Board of Directors shall be and is divided into three classes, designated Class I, Class II and Class III. Each class shall consist, as nearly as may be possible, of one-third of the total number of directors constituting the entire Board of Directors. The Board of Directors is authorized to assign members of the Board of Directors already in office to Class I, Class II or Class III at the time such classification becomes effective.

4. Terms of Office. Subject to the rights of holders of any series of Preferred Stock to elect directors, each director shall serve for a term ending on the date of the third annual meeting of stockholders following the annual meeting of stockholders at which such director was elected; provided that each director initially assigned to Class I shall serve for a term expiring at the Corporation's first annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; each director initially assigned to Class II shall serve for a term expiring at the Corporation's second annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; and each director initially assigned to Class III shall serve for a term expiring at the Corporation's third annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; provided further, that the term of each director shall continue until the election and qualification of his or her successor and be subject to his or her earlier death, resignation or removal.

5. Quorum. The greater of (a) a majority of the directors at any time in office and (b) one-third of the number of directors fixed pursuant to Section 2 of this Article NINTH shall constitute a quorum of the Board of Directors. If at any meeting of the Board of Directors there shall be less than such a quorum, a majority of the directors present may adjourn the meeting from time to time without further notice other than announcement at the meeting, until a quorum shall be present.

6. Action at Meeting. Every act or decision done or made by a majority of the directors present at a meeting duly held at which a quorum is present shall be regarded as the act of the Board of Directors unless a greater number is required by law or by this Certificate of Incorporation.

7. Removal. Subject to the rights of holders of any series of Preferred Stock, directors of the Corporation may be removed only for cause and only by the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors.

8. Vacancies. Subject to the rights of holders of any series of Preferred Stock, any vacancy or newly created directorship in the Board of Directors, however occurring, shall be filled only by vote of a majority of the directors then in office, although less than a quorum, or by a sole remaining director and shall not be filled by the stockholders. A director elected to fill a vacancy shall hold office until the next election of the class for which such director shall have been chosen, subject to the election and qualification of a successor and to such director's earlier death, resignation or removal.

9. Stockholder Nominations and Introduction of Business, Etc. Advance notice of stockholder nominations for election of directors and other business to be brought by stockholders before a meeting of stockholders shall be given in the manner provided by the By-laws of the Corporation.

10. Amendments to Article. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article NINTH.

TENTH: Stockholders of the Corporation may not take any action by written consent in lieu of a meeting. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article TENTH.

ELEVENTH: Special meetings of stockholders for any purpose or purposes may be called at any time by only the Board of Directors, the Chairman of the Board or the Chief Executive Officer, and may not be called by any other person or persons. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article ELEVENTH.

IN WITNESS WHEREOF, this Restated Certificate of Incorporation, which restates, integrates and amends the certificate of incorporation of the Corporation, and which has been duly adopted in accordance with Sections 228, 242 and 245 of the General Corporation Law of the State of Delaware, has been executed by its duly authorized officer this 6th day of July, 2016.

SYROS PHARMACEUTICALS, INC.

By: /s/Nancy Simonian, M.D.
Name: Nancy Simonian, M.D.
Title: President and Chief Executive Officer

SYROS PHARMACEUTICALS, INC.

**CERTIFICATE OF DESIGNATION OF PREFERENCES,
RIGHTS AND LIMITATIONS
OF
SERIES A CONVERTIBLE PREFERRED STOCK**

PURSUANT TO SECTION 151 OF THE
DELAWARE GENERAL CORPORATION LAW

SYROS PHARMACEUTICALS, INC., a Delaware corporation (the "**Corporation**"), in accordance with the provisions of Section 103 of the Delaware General Corporation Law (the "**DGCL**") does hereby certify that, in accordance with Sections 141(c) and 151 of the DGCL, the following resolution was duly adopted by the Board of Directors of the Corporation on April 4, 2019:

RESOLVED, pursuant to authority expressly set forth in the Restated Certificate of Incorporation of the Corporation (the "**Certificate of Incorporation**"), the issuance of a series of Preferred Stock designated as the Series A Convertible Preferred Stock, par value $0.001 per share, of the Corporation is hereby authorized and the designation, number of shares, powers, preferences, rights, qualifications, limitations and restrictions thereof (in addition to any provisions set forth in the Certificate of Incorporation that are applicable to the Preferred Stock of all classes and series) are hereby fixed, and the Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock is hereby approved as follows:

SERIES A CONVERTIBLE PREFERRED STOCK

Section 1. Definitions. For the purposes hereof, the following terms shall have the following meanings:

"**Affiliate**" means any person or entity that, directly or indirectly through one or more intermediaries, controls or is controlled by or is under common control with a person or entity, as such terms are used in and construed under Rule 144 under the Securities Act. With respect to a Holder, any investment fund or managed account that is managed on a discretionary basis by the same investment manager as such Holder will be deemed to be an Affiliate of such Holder.

"**Alternate Consideration**" shall have the meaning set forth in Section 7(b).

"**Beneficial Ownership Limitation**" shall have the meaning set forth in Section 6(c).

"**Business Day**" means any day except Saturday, Sunday, any day which shall be a federal legal holiday in the United States or any day on which banking institutions in the State of New York are authorized or required by law or other governmental action to close.

"**Buy-In**" shall have the meaning set forth in Section 6(d)(iii).

"**Closing Sale Price**" means, for any security as of any date, the last closing trade price for such security prior to 4:00 p.m., New York City time, on the principal securities exchange or

trading market where such security is listed or traded, as reported by Bloomberg, L.P. (or an equivalent, reliable reporting service mutually acceptable to and hereafter designated by Holders of a majority of the then-outstanding Series A Preferred Stock and the Corporation), or if the foregoing do not apply, the last trade price of such security in the over-the-counter market on the electronic bulletin board for such security as reported by Bloomberg, L.P., or, if no last trade price is reported for such security by Bloomberg, L.P., the average of the bid prices of any market makers for such security as reported on the OTC Pink Market by OTC Markets Group, Inc. If the Closing Sale Price cannot be calculated for a security on a particular date on any of the foregoing bases, the Closing Sale Price of such security on such date shall be the fair market value as determined in good faith by the Board of Directors of the Corporation.

"**Commission**" means the Securities and Exchange Commission.

"**Common Stock**" means the Corporation's common stock, par value $0.001 per share, and stock of any other class of securities into which such common stock may hereafter be reclassified or changed into.

"**Conversion Date**" shall have the meaning set forth in Section 6(a).

"**Conversion Price**" shall mean $7.50, as adjusted pursuant to paragraph 7 hereof.

"**Conversion Ratio**" shall have the meaning set forth in Section 6(b).

"**Conversion Shares**" means, collectively, the shares of Common Stock issuable upon conversion of the shares of Series A Preferred Stock in accordance with the terms hereof.

"**Daily Failure Amount**" means the product of (x) .005 multiplied by (y) the Closing Sale Price of the Common Stock on the applicable Share Delivery Date.

"**DGCL**" shall mean the Delaware General Corporation Law.

"**Distributions**" shall have the meaning set forth in Section 5(a).

"**DTC**" shall have the meaning set forth in Section 6(a).

"**DWAC Delivery**" shall have the meaning set forth in Section 6(a).

"**Exchange Act**" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

"**Fundamental Transaction**" shall have the meaning set forth in Section 7(b).

"**Holder**" means any holder of Series A Preferred Stock.

"**Issuance Date**" means April 9, 2019.

"**Junior Securities**" shall have the meaning set forth in Section 5(a).

"**Notice of Conversion**" shall have the meaning set forth in Section 6(a).

"**Parity Securities**" shall have the meaning set forth in Section 5(a).

"**Person**" means any individual or corporation, partnership, trust, incorporated or unincorporated association, joint venture, limited liability company, joint stock company, government (or an agency or subdivision thereof) or other entity of any kind.

"**Securities Act**" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

"**Senior Securities**" shall have the meaning set forth in Section 5(a).

"**Series A Preferred Stock**" shall have the meaning set forth in Section 2(a).

"**Series A Preferred Stock Register**" shall have the meaning set forth in Section 2(b).

"**Share Delivery Date**" shall have the meaning set forth in Section 6(d)(i).

"**Stated Value**" shall mean $7,500.

"**Trading Day**" means a day on which the Common Stock is traded for any period on the principal securities exchange or if the Common Stock is not traded on a principal securities exchange, on a day that the Common Stock is traded on another securities market on which the Common Stock is then being traded.

Section 2. Designation, Amount and Par Value; Assignment.

(a) The series of preferred stock designated by this Certificate of Designation shall be designated as the Corporation's Series A Convertible Preferred Stock (the "**Series A Preferred Stock**") and the number of shares so designated shall be 666. Each share of Series A Preferred Stock shall have a par value of $0.001 per share. The Series A Preferred Stock may be issued in certificated form or in book-entry form at the election of the Holder. To the extent that any shares of Series A Preferred Stock are issued in book-entry form, references herein to "certificates" shall instead refer to the book-entry notation relating to such shares.

(b) The Corporation shall register shares of the Series A Preferred Stock, upon records to be maintained by the Corporation for that purpose (the "**Series A Preferred Stock Register**"), in the name of the Holders thereof from time to time. The Corporation may deem and treat the registered Holder of shares of Series A Preferred Stock as the absolute owner thereof for the purpose of any conversion thereof and for all other purposes. The Corporation shall register the transfer of any shares of Series A Preferred Stock in the Series A Preferred Stock Register, upon surrender of the certificates evidencing such shares to be transferred, duly endorsed by the Holder thereof, to the Corporation at its address specified herein. Upon any such registration or transfer, a new certificate evidencing the shares of Series A Preferred Stock so transferred shall be issued to the transferee and a new certificate evidencing the remaining portion of the shares not so transferred, if any, shall be issued to the transferring Holder, in each case, within three (3) Business Days. The provisions of this Certificate of Designation are intended to be for the benefit of all Holders from time to time and shall be enforceable by any such Holder.

Section 3. Dividends. Holders shall be entitled to receive, and the Corporation shall pay, dividends on shares of the Series A Preferred Stock equal (on an as-if-converted-to-Common-Stock basis, without regard to the Beneficial Ownership Limitation) to and in the same form, and

in the same manner, as dividends (other than dividends in the form of Common Stock) actually paid on shares of the Common Stock when, as and if such dividends (other than dividends in the form of Common Stock, which shall be made in accordance with Section 7(a)) are paid on shares of the Common Stock. Other than as set forth in the previous sentence, no other dividends shall be paid on shares of Series A Preferred Stock, and the Corporation shall pay no dividends (other than dividends in the form of Common Stock) on shares of the Common Stock unless it simultaneously complies with the previous sentence.

Section 4. Voting Rights; Amendments. Except as otherwise provided herein or as otherwise required by the DGCL, the Series A Preferred Stock shall have no voting rights. However, as long as any shares of Series A Preferred Stock are outstanding, the Corporation shall not, without the affirmative vote of the Holders of a majority of the then outstanding shares of the Series A Preferred Stock, (a) (i) alter or change adversely the powers, preferences or rights given to the Series A Preferred Stock, (ii) alter or amend this Certificate of Designation, or (iii) amend or repeal any provision of, or add any provision to, the Certificate of Incorporation or bylaws of the Corporation, or file any articles of amendment or certificate of designations of preferences, limitations and relative rights of any series of preferred stock, if such action would adversely alter or change the powers, preferences or rights of the Series A Preferred Stock in a manner materially different than the effect of such actions on the Common Stock (regardless, in the case of clause (i), (ii) or (iii), of whether any of the foregoing actions shall be by means of amendment to the Certificate of Incorporation or by merger, consolidation or otherwise), (b) issue further shares of Series A Preferred Stock or increase or decrease (other than by conversion) the number of authorized shares of Series A Preferred Stock or (c) enter into any agreement with respect to any of the foregoing.

Section 5. Rank; Liquidation.

(a) The Series A Preferred Stock shall rank (i) senior to all of the Common Stock; (ii) senior to any class or series of capital stock of the Corporation hereafter created specifically ranking by its terms junior to any Series A Preferred Stock ("**Junior Securities**"); (iii) on parity with any class or series of capital stock of the Corporation hereafter created specifically ranking by its terms on parity with the Series A Preferred Stock (the "**Parity Securities**"); and (iv) junior to any class or series of capital stock of the Corporation hereafter created specifically ranking by its terms senior to any Series A Preferred Stock ("**Senior Securities**"), in each case, as to distributions of assets upon liquidation, dissolution or winding up of the Corporation, whether voluntarily or involuntarily (all such distributions being referred to collectively as "**Distributions**").

(b) Subject to the prior and superior rights of the holders of any Senior Securities of the Corporation, upon liquidation, dissolution or winding up of the Corporation, whether voluntary or involuntary, each holder of shares of Series A Preferred Stock shall be entitled to receive, in preference to any distributions of any of the assets or surplus funds of the Corporation to the holders of the Common Stock and Junior Securities and *pari passu* with any distribution to the holders of Parity Securities, an amount equal to $0.001 per share of Series A Preferred Stock, plus an additional amount equal to any dividends declared but unpaid on such shares, before any payments shall be made or any assets distributed to holders of any class of Common Stock or Junior Securities. If, upon any such liquidation, dissolution or winding up of the Corporation, the assets of the Corporation shall be insufficient to pay the holders of shares of the Series A Preferred Stock the amount required under the preceding sentence, then all remaining assets of the Corporation shall be distributed ratably to holders of the shares of the Series A Preferred Stock and Parity Securities in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

Section 6. Conversion.

(a) Conversions at Option of Holder. Each share of Series A Preferred Stock shall be convertible, at any time and from time to time from and after the Issuance Date, at the option of the Holder thereof, into a number of shares of Common Stock equal to the Conversion Ratio. Holders shall effect conversions by providing the Corporation with the form of conversion notice attached hereto as **Annex A** (a "**Notice of Conversion**"), duly completed and executed. Other than a conversion following a Fundamental Transaction or following a notice provided for under Section 7(d)(ii) hereof, the Notice of Conversion must specify at least a number of shares of Series A Preferred Stock to be converted equal to the lesser of (x) 10,000 shares (such number subject to appropriate adjustment following the occurrence of an event specified in Section 7(a) hereof) and (y) the number of shares of Series A Preferred Stock then held by the Holder. Provided the Corporation's transfer agent is participating in the Depository Trust Company ("**DTC**") Fast Automated Securities Transfer program, the Notice of Conversion may specify, at the Holder's election, whether the applicable Conversion Shares shall be credited to the account of the Holder's prime broker with DTC through its Deposit Withdrawal Agent Commission system (a "**DWAC Delivery**"). The "**Conversion Date**", or the date on which a conversion shall be deemed effective, shall be defined as the Trading Day that the Notice of Conversion, completed and executed, is sent by facsimile or other electronic transmission to, and received during regular business hours by, the Corporation; provided that the original certificate(s) (if applicable) representing such shares of Series A Preferred Stock being converted, duly endorsed, and the accompanying Notice of Conversion, are received by the Corporation within two (2) Trading Days thereafter. In all other cases, the Conversion Date shall be defined as the Trading Day on which the original share certificate(s) (if applicable) of Series A Preferred Stock being converted, duly endorsed, and the accompanying Notice of Conversion, are received by the Corporation. The calculations set forth in the Notice of Conversion shall control in the absence of manifest or mathematical error.

(b) Conversion Ratio. The "**Conversion Ratio**" for each share of Series A Preferred Stock shall be equal to the Stated Value divided by the Conversion Price.

(c) Beneficial Ownership Limitation. Notwithstanding anything herein to the contrary, the Corporation shall not effect any conversion of the Series A Preferred Stock, and a Holder shall not have the right to convert any portion of the Series A Preferred Stock, to the extent that, after giving effect to an attempted conversion set forth on an applicable Notice of Conversion, such Holder (together with such Holder's Affiliates, and any other Person whose beneficial ownership of Common Stock would be aggregated with the Holder's for purposes of Section 13(d) or Section 16 of the Exchange Act and the applicable regulations of the Commission, including any "group" of which the Holder is a member (the foregoing, "**Attribution Parties**")) would beneficially own a number of shares of Common Stock in excess of the Beneficial Ownership Limitation (as defined below). For purposes of the foregoing sentence, the aggregate number of shares of Common Stock beneficially owned by such Holder and its Attribution Parties shall include the number of shares of Common Stock held by such Holder and its Attribution Parties plus the number of shares of Common Stock issuable upon conversion of the Series A Preferred Stock subject to the Notice of Conversion with respect to which such determination is being made, but shall exclude the number of shares of Common Stock which are issuable upon (A) conversion of the remaining, unconverted shares of Series A Preferred Stock beneficially owned by such Holder or any of its Attribution Parties, and (B) exercise or conversion of the unexercised or unconverted portion of any other securities of the Corporation (including any warrants) beneficially owned by such Holder or any of its Attribution Parties that, in the case of both (A) and (B), are subject to a limitation on conversion or exercise similar to the limitation contained herein. For purposes of this Section 6(c), beneficial ownership shall be calculated in accordance with Section 13(d) of the Exchange Act and the applicable regulations of the Commission. In addition, for purposes hereof, "group" has the meaning set forth in Section 13(d) of the Exchange Act and the applicable regulations of the Commission. For purposes of this Section 6(c), in determining the number of outstanding shares of Common Stock, a Holder may rely on the number of outstanding shares of Common Stock as stated in the most recent of the following: (A) the Corporation's most recent periodic or annual filing with the Commission, as the case may be, (B) a more recent public announcement by the Corporation that is filed with the Commission, or (C) a more recent notice by the Corporation or the Corporation's transfer agent to the Holder setting forth the number of shares of Common Stock then outstanding. Upon the written request of a Holder (which may be by email), the Corporation shall, within three (3) Trading Days thereof, confirm in writing to such Holder (which may be via email) the number of shares of Common Stock then outstanding. In any case, the number of outstanding shares of Common Stock shall be determined after giving effect to any actual conversion or exercise of securities of the Corporation, including shares of Series A Preferred Stock, by such Holder or its Attribution Parties since the date as of which such number of outstanding shares of Common Stock was last publicly reported or confirmed to the Holder. The "**Beneficial Ownership Limitation**" shall initially be 9.99% of the number of shares of the Common Stock outstanding immediately after giving effect to the issuance of shares of Common Stock pursuant to such Notice of Conversion (to the extent permitted pursuant to this Section 6(c)). Notwithstanding the foregoing, by written notice to the Corporation, which will not be effective until the sixty-first (61st) day after such notice is delivered to the Corporation, the Holder may reset the Beneficial Ownership Limitation percentage to a higher or lower percentage. Upon such a change by a Holder of the Beneficial Ownership Limitation, the Beneficial Ownership Limitation may not be further amended by such Holder without first providing the minimum 61-day notice required by this Section 6(c). Notwithstanding the

foregoing, at any time following notice of a Fundamental Transaction, the Holder may waive and/or change the Beneficial Ownership Limitation effective immediately upon written notice to the Corporation and may reinstitute a Beneficial Ownership Limitation at any time thereafter effective immediately upon written notice to the Corporation. The Corporation shall be entitled to rely on representations made to it by the Holder in any Notice of Conversion regarding its Beneficial Ownership Limitation, and the determination as to whether the Series A Preferred Stock is convertible and of which portion of the Series A Preferred Stock is convertible shall be made in the sole discretion of the Holder and the Company shall have no obligation to verify or confirm the accuracy of such determination.

(d) Mechanics of Conversion

(i) Delivery of Certificate or Electronic Issuance Upon Conversion. Not later than three (3) Trading Days after the applicable Conversion Date, or if the Holder requests the issuance of physical certificate(s), two (2) Trading Days after receipt by the Corporation of both the original certificate(s) representing such shares of Series A Preferred Stock being converted, duly endorsed, and the accompanying Notice of Conversion (the "**Share Delivery Date**"), the Corporation shall (a) deliver, or cause to be delivered, to the converting Holder a physical certificate or certificates representing the number of Conversion Shares being acquired upon the conversion of shares of Series A Preferred Stock or (b) in the case of a DWAC Delivery, electronically transfer such Conversion Shares by crediting the account of the Holder's prime broker with DTC through its DWAC system. If in the case of any Notice of Conversion such certificate or certificates are not delivered to or as directed by or, in the case of a DWAC Delivery, such shares are not electronically delivered to or as directed by, the applicable Holder by the Share Delivery Date, the applicable Holder shall be entitled to elect to rescind such Notice of Conversion by written notice to the Corporation at any time on or before its receipt of such certificate or certificates for Conversion Shares or electronic receipt of such shares, as applicable, in which event the Corporation shall promptly return to such Holder any original Series A Preferred Stock certificate delivered to the Corporation and such Holder shall promptly return to the Corporation any Common Stock certificates or otherwise direct the return of any shares of Common Stock delivered to the Holder through the DWAC system, representing the shares of Series A Preferred Stock unsuccessfully tendered for conversion to the Corporation.

(ii) Obligation Absolute. Subject to Section 6(c) hereof and subject to Holder's right to rescind a Notice of Conversion pursuant to Section 6(d)(i) above, the Corporation's obligation to issue and deliver the Conversion Shares upon conversion of Series A Preferred Stock in accordance with the terms hereof are absolute and unconditional, irrespective of any action or inaction by a Holder to enforce the same, any waiver or consent with respect to any provision hereof, the recovery of any judgment against any Person or any action to enforce the same, or any setoff, counterclaim, recoupment, limitation or termination, or any breach or alleged breach by such Holder or any other Person of any obligation to the Corporation or any violation or alleged violation of law by such Holder or any other Person, and irrespective of any other circumstance which might otherwise limit such obligation of the Corporation to such Holder in connection with the issuance of such Conversion Shares. Subject to Section 6(c) hereof and subject to Holder's right to rescind a Notice of Conversion pursuant to Section 6(d)(i) above, in the event a Holder shall elect to convert any or all of its Series A Preferred Stock, the Corporation may not refuse conversion based on any claim that such Holder or anyone

associated or affiliated with such Holder has been engaged in any violation of law, agreement or for any other reason, unless an injunction from a court, on notice to Holder, restraining and/or enjoining conversion of all or part of the Series A Preferred Stock of such Holder shall have been sought and obtained by the Corporation, and the Corporation posts a surety bond for the benefit of such Holder in the amount of 150% of the value of the Conversion Shares into which would be converted the Series A Preferred Stock which is subject to such injunction, which bond shall remain in effect until the completion of arbitration/litigation of the underlying dispute and the proceeds of which shall be payable to such Holder to the extent it obtains judgment. In the absence of such injunction, the Corporation shall, subject to Section 6(c) hereof and subject to Holder's right to rescind a Notice of Conversion pursuant to Section 6(d)(i) above, issue Conversion Shares upon a properly noticed conversion. If the Corporation fails to deliver to a Holder such certificate or certificates, or electronically deliver (or cause its transfer agent to electronically deliver) such shares in the case of a DWAC Delivery, pursuant to Section 6(d)(i) on or prior to the fifth (5th) Trading Day after the Share Delivery Date applicable to such conversion (other than a failure caused by incorrect or incomplete information provided by Holder to the Corporation), then, unless the Holder has rescinded the applicable Notice of Conversion pursuant to Section 6(d)(i) above, the Corporation shall pay (as liquidated damages and not as a penalty) to such Holder an amount payable, at the Holder's option, either (a) in cash or (b) to the extent that it would not cause the Holder or its Attribution Parties to exceed the Beneficial Ownership Limitation, in shares of Common Stock that are valued for these purposes at the Closing Sale Price on the date of such calculation, in each case equal to the product of (x) the number of Conversion Shares required to have been issued by the Corporation on such Share Delivery Date, (y) an amount equal to the Daily Failure Amount and (z) the number of Trading Days actually lapsed after such fifth (5th) Trading Day after the Share Delivery Date during which such certificates have not been delivered, or, in the case of a DWAC Delivery, such shares have not been electronically delivered; *provided*, *however*, the Holder shall only receive up to such amount of shares of Common Stock such that Holder and its Attribution Parties and any other persons or entities whose beneficial ownership of Common Stock would be aggregated with the Holder's for purposes of Section 13(d) of the Exchange Act (including shares held by any "group" of which the Holder is a member, but excluding shares beneficially owned by virtue of the ownership of securities or rights to acquire securities that have limitations on the right to convert, exercise or purchase similar to the limitation set forth herein) shall not collectively beneficially own greater than the Beneficial Ownership Limitation. Nothing herein shall limit a Holder's right to pursue actual damages for the Corporation's failure to deliver Conversion Shares within the period specified herein and such Holder shall have the right to pursue all remedies available to it hereunder, at law or in equity including, without limitation, a decree of specific performance and/or injunctive relief; provided that Holder shall not receive duplicate damages for the Corporation's failure to deliver Conversion Shares within the period specified herein. The exercise of any such rights shall not prohibit a Holder from seeking to enforce damages pursuant to any other Section hereof or under applicable law.

(iii) Compensation for Buy-In on Failure to Timely Deliver Certificates Upon Conversion. If the Corporation fails to deliver to a Holder the applicable certificate or certificates or to effect a DWAC Delivery, as applicable, by the Share Delivery Date pursuant to Section 6(d)(i) (other than a failure caused by incorrect or incomplete information provided by Holder to the Corporation), and if after such Share Delivery Date such Holder is required by its brokerage firm to purchase (in an open market transaction or otherwise), or the Holder's brokerage firm

otherwise purchases, shares of Common Stock to deliver in satisfaction of a sale by such Holder of the Conversion Shares which such Holder was entitled to receive upon the conversion relating to such Share Delivery Date (a "**Buy-In**"), then the Corporation shall (A) pay in cash to such Holder (in addition to any other remedies available to or elected by such Holder) the amount by which (x) such Holder's total purchase price (including any brokerage commissions) for the shares of Common Stock so purchased exceeds (y) the product of (1) the aggregate number of shares of Common Stock that such Holder was entitled to receive from the conversion at issue multiplied by (2) the actual sale price at which the sell order giving rise to such purchase obligation was executed (including any brokerage commissions) and (B) at the option of such Holder, either reissue (if surrendered) the shares of Series A Preferred Stock equal to the number of shares of Series A Preferred Stock submitted for conversion or deliver to such Holder the number of shares of Common Stock that would have been issued if the Corporation had timely complied with its delivery requirements under Section 6(d)(i). For example, if a Holder purchases shares of Common Stock having a total purchase price of $11,000 to cover a Buy-In with respect to an attempted conversion of shares of Series A Preferred Stock with respect to which the actual sale price (including any brokerage commissions) giving rise to such purchase obligation was a total of $10,000 under clause (A) of the immediately preceding sentence, the Corporation shall be required to pay such Holder $1,000. The Holder shall provide the Corporation written notice, within three (3) Trading Days after the occurrence of a Buy-In, indicating the amounts payable to such Holder in respect of such Buy-In together with applicable confirmations and other evidence reasonably requested by the Corporation. Nothing herein shall limit a Holder's right to pursue any other remedies available to it hereunder, at law or in equity including, without limitation, a decree of specific performance and/or injunctive relief with respect to the Corporation's failure to timely deliver certificates representing shares of Common Stock upon conversion of the shares of Series A Preferred Stock as required pursuant to the terms hereof; provided, however, that the Holder shall not be entitled to both (i) require the reissuance of the shares of Series A Preferred Stock submitted for conversion for which such conversion was not timely honored and (ii) receive the number of shares of Common Stock that would have been issued if the Corporation had timely complied with its delivery requirements under Section 6(d)(i).

(iv) Reservation of Shares Issuable Upon Conversion. The Corporation covenants that it will at all times reserve and keep available out of its authorized and unissued shares of Common Stock for the sole purpose of issuance upon conversion of the Series A Preferred Stock, free from preemptive rights or any other actual contingent purchase rights of Persons other than the Holders of the Series A Preferred Stock, not less than such aggregate number of shares of the Common Stock as shall be issuable (taking into account the adjustments of Section 7) upon the conversion of all outstanding shares of Series A Preferred Stock. The Corporation covenants that all shares of Common Stock that shall be so issuable shall, upon issue, be duly authorized, validly issued, fully paid, nonassessable and free and clear of all liens and other encumbrances.

(v) Fractional Shares. No fractional shares or scrip representing fractional shares of Common Stock shall be issued upon the conversion of the Series A Preferred Stock. As to any fraction of a share which a Holder would otherwise be entitled to receive upon such conversion, the Corporation shall pay a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the Conversion Price.

(vi) Transfer Taxes. The issuance of certificates for shares of the Common Stock upon conversion of the Series A Preferred Stock shall be made without charge to any Holder for any documentary stamp or similar taxes that may be payable in respect of the issue or delivery of such certificates, provided that the Corporation shall not be required to pay any tax that may be payable in respect of any transfer involved in the issuance and delivery of any such certificate upon conversion in a name other than that of the registered Holder(s) of such shares of Series A Preferred Stock and the Corporation shall not be required to issue or deliver such certificates unless or until the Person or Persons requesting the issuance thereof shall have paid to the Corporation the amount of such tax or shall have established to the satisfaction of the Corporation that such tax has been paid.

(e) Status as Stockholder. Upon each Conversion Date, (i) the shares of Series A Preferred Stock being converted shall be deemed converted into shares of Common Stock and (ii) the Holder's rights as a holder of such converted shares of Series A Preferred Stock shall cease and terminate, excepting only the right to receive certificates for such shares of Common Stock and to any remedies provided herein or otherwise available at law or in equity to such Holder because of a failure by the Corporation to comply with the terms of this Certificate of Designation. In all cases, the Holder shall retain all of its rights and remedies for the Corporation's failure to convert Series A Preferred Stock.

Section 7. Certain Adjustments.

(a) Stock Dividends and Stock Splits. If the Corporation, at any time while this Series A Preferred Stock is outstanding: (i) pays a stock dividend or otherwise makes a distribution or distributions payable in shares of Common Stock (which, for avoidance of doubt, shall not include any shares of Common Stock issued by the Corporation upon conversion of this Series A Preferred Stock) with respect to the then outstanding shares of Common Stock; (ii) subdivides outstanding shares of Common Stock into a larger number of shares; or (iii) combines (including by way of a reverse stock split) outstanding shares of Common Stock into a smaller number of shares, then the Conversion Price shall be multiplied by a fraction of which the numerator shall be the number of shares of Common Stock (excluding any treasury shares of the Corporation) outstanding immediately before such event and of which the denominator shall be the number of shares of Common Stock outstanding immediately after such event (excluding any treasury shares of the Corporation). Any adjustment made pursuant to this Section 7(a) shall become effective immediately after the record date for the determination of stockholders entitled to receive such dividend or distribution and shall become effective immediately after the effective date in the case of a subdivision or combination.

(b) Fundamental Transaction. If, at any time while this Series A Preferred Stock is outstanding, (i) the Corporation, directly or indirectly in one or more related transactions, effects any merger or consolidation of the Corporation with or into another Person (other than such a transaction in which the Corporation is the surviving or continuing entity and its Common Stock is not exchanged for or converted into other securities, cash or property), (ii) the Corporation directly or indirectly effects any sale, lease, license, assignment, transfer, conveyance or other disposition of all or substantially all of its assets in one transaction or a series of related transactions, (iii) any tender offer or exchange offer (whether by the Corporation or another Person) is completed pursuant to which more than 50% of the Common Stock not held by the

Corporation or such Person is exchanged for or converted into other securities, cash or property, (iv) the Corporation, directly or indirectly in one or more related transactions, effects any reclassification, reorganization or recapitalization of the Common Stock or any compulsory share exchange pursuant (other than as a result of a dividend, subdivision or combination covered by Section 7(a) above) to which the Common Stock is effectively converted into or exchanged for other securities, cash or property, or (v) the Corporation, directly or indirectly, in one or more related transactions consummates a stock or share purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off or scheme of arrangement) with another Person whereby such other Person acquires more than 50% of the outstanding shares of Common Stock (not including any shares of Common Stock held by the other Person or other Persons making or party to, or associated or affiliated with the other Persons making or party to, such stock or share purchase agreement or other business combination and excluding shares acquired upon conversion of any currently outstanding convertible securities in accordance with the terms thereof as in effect on the date hereof) (in any such case, a "**Fundamental Transaction**"), then, as of the effective date and time of the Fundamental Transaction (the "**Effective Time**"), each outstanding share of Series A Preferred Stock shall be canceled without any further action on the part of the Corporation or the Holder thereof, and in consideration for such cancellation, each Holder shall automatically receive, for each Conversion Share that would have been issuable upon conversion of such cancelled shares of Series A Preferred Stock immediately prior to the occurrence of such Fundamental Transaction, the same kind and amount of securities, cash or property receivable upon the effectiveness of the Fundamental Transaction ("**Exchange Property**") as it would have been entitled to receive upon the occurrence of such Fundamental Transaction if it had been, immediately prior to such Fundamental Transaction, the holder of one share of Common Stock (the "**Alternate Consideration**"); provided, however, if the Fundamental Transaction is not of a type that results in the Common Stock being exchanged for other securities, cash or property, then the Series A Preferred Stock shall not be cancelled as provided in the immediately preceding sentence and shall remain outstanding. The amount of Exchange Property receivable upon any Fundamental Transaction shall be determined based upon the Conversion Ratio in effect at such Effective Time. Upon the cancellation of any Series A Preferred Stock as of the Effective Time, the Holder's rights as a holder of Series A Preferred Stock shall cease and terminate, excepting only the right to receive the Exchange Property to which the Holder is then entitled and to any remedies provided herein or otherwise available at law or in equity to such Holder because of a failure by the Corporation to comply with the terms of this Certificate of Designation. Should any shares of Series A Preferred Stock remain outstanding after a Fundamental Transaction, for purposes of any such subsequent conversion, the determination of the Conversion Ratio shall be appropriately adjusted to apply to such Alternate Consideration, if any, based on the amount of Alternate Consideration issuable in respect of one share of Common Stock in such Fundamental Transaction, and the Corporation shall adjust the Conversion Ratio in a reasonable manner reflecting the relative value of any different components of the Alternate Consideration. If holders of Common Stock are given any choice as to the securities, cash or property to be received in a Fundamental Transaction, then the Holders shall be given the same choice as to the Alternate Consideration it receives upon any conversion of their shares of Series A Preferred Stock following such Fundamental Transaction should such shares of Series A Preferred Stock remain outstanding after such Fundamental Transaction. To the extent necessary to effectuate the foregoing provisions should any shares of Series A Preferred Stock remain

outstanding after a Fundamental Transaction, any successor to the Corporation or surviving entity in such Fundamental Transaction shall file a new Certificate of Designation with the same terms and conditions and issue to the Holders new preferred stock consistent with the foregoing provisions and evidencing the Holders' right to convert such preferred stock into Alternate Consideration. The terms of any agreement to which the Corporation is a party and pursuant to which a Fundamental Transaction is effected shall include terms requiring any such successor or surviving entity to comply with the provisions of this Section 7(b) and ensuring that this Series A Preferred Stock (or any such replacement security) will be similarly adjusted upon any subsequent transaction analogous to a Fundamental Transaction. The Corporation shall cause to be delivered to each Holder, at its last address as it shall appear upon the stock books of the Corporation, written notice of any Fundamental Transaction at least 20 calendar days prior to the date on which such Fundamental Transaction is expected to become effective or close, which notice shall state the kind and amount of cash, securities or property that constitute the Exchange Property. Failure to deliver such notice shall not affect the operation of this Section 7. The Corporation shall not enter into any agreement for a transaction constituting a Fundamental Transaction that would interfere with or prevent (as applicable) the treatment of the Series A Preferred Stock in a manner that is consistent with and gives effect to this Section 7.

(c) Calculations. All calculations under this Section 7 shall be made to the nearest cent or the nearest 1/100th of a share, as the case may be. For purposes of this Section 7, the number of shares of Common Stock deemed to be issued and outstanding as of a given date shall be the sum of the number of shares of Common Stock (excluding any treasury shares of the Corporation) issued and outstanding.

(d) Notice to the Holders.

(i) Adjustment to Conversion Price. Whenever the Conversion Price is adjusted pursuant to any provision of this Section 7, the Corporation shall promptly deliver to each Holder a notice setting forth the Conversion Ratio after such adjustment and setting forth a brief statement of the facts requiring such adjustment.

(ii) Other Notices. If (A) the Corporation shall declare a dividend (or any other distribution in whatever form) on the Common Stock, (B) the Corporation shall declare a special nonrecurring cash dividend on or a redemption of the Common Stock, (C) the Corporation shall authorize the granting to all holders of the Common Stock of rights or warrants to subscribe for or purchase any shares of capital stock of any class or of any rights, (D) the approval of any stockholders of the Corporation shall be required in connection with any reclassification of the Common Stock, any consolidation or merger to which the Corporation is a party, any sale or transfer of all or substantially all of the assets of the Corporation, or any compulsory share exchange whereby the Common Stock is converted into other securities, cash or property, or (E) the Corporation shall authorize the voluntary or involuntary dissolution, liquidation or winding up of the affairs of the Corporation, then, in each case, the Corporation shall cause to be filed at each office or agency maintained for the purpose of conversion of this Series A Preferred Stock, and, except if such notice and the contents thereof shall be deemed to constitute material non-public information, shall cause to be delivered to each Holder at its last address as it shall appear upon the stock books of the Corporation, at least 20 calendar days prior to the applicable record or effective date hereinafter specified, a notice stating (x) the date on which a record is to be

taken for the purpose of such dividend, distribution, redemption, rights or warrants, or if a record is not to be taken, the date as of which the holders of the Common Stock of record to be entitled to such dividend, distributions, redemption, rights or warrants are to be determined or (y) the date on which such reclassification, consolidation, merger, sale, transfer or share exchange is expected to become effective or close, and the date as of which it is expected that holders of the Common Stock of record shall be entitled to exchange their shares of the Common Stock for securities, cash or other property deliverable upon such reclassification, consolidation, merger, sale, transfer or share exchange, provided that the failure to deliver such notice or any defect therein or in the delivery thereof shall not affect the validity of the corporate action required to be specified in such notice.

Section 8. Miscellaneous.

(a) Notices. Any and all notices or other communications or deliveries to be provided by the Holders hereunder including, without limitation, any Notice of Conversion, shall be in writing and delivered personally, by facsimile, via email or sent by a nationally recognized overnight courier service, addressed to the Corporation, at 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139, Attention: Nancy Simonian, M.D., email: nsimonian@syros.com, or such other email address or mailing address as the Corporation may specify for such purposes by notice to the Holders delivered in accordance with this Section. Any and all notices or other communications or deliveries to be provided by the Corporation hereunder shall be in writing and delivered personally, by facsimile, or sent by a nationally recognized overnight courier service addressed to each Holder at the facsimile number or address of such Holder appearing on the books of the Corporation, or if no such facsimile number or address appears on the books of the Corporation, at the principal place of business of such Holder. Any notice or other communication or deliveries hereunder shall be deemed given and effective on the earliest of (i) the date of transmission, if such notice or communication is delivered via facsimile at the facsimile number, or via email at the email address, specified in this Section prior to 5:30 p.m. (New York City time) on any date, (ii) the date immediately following the date of transmission, if such notice or communication is delivered via facsimile at the facsimile number, or via email at the email address, specified in this Section between 5:30 p.m. and 11:59 p.m. (New York City time) on any date, (iii) the second Business Day following the date of mailing, if sent by nationally recognized overnight courier service, or (iv) upon actual receipt by the party to whom such notice is required to be given.

(b) Lost or Mutilated Series A Preferred Stock Certificate. If a Holder's Series A Preferred Stock certificate shall be mutilated, lost, stolen or destroyed, the Corporation shall execute and deliver, in exchange and substitution for and upon cancellation of a mutilated certificate, or in lieu of or in substitution for a lost, stolen or destroyed certificate, a new certificate for the shares of Series A Preferred Stock so mutilated, lost, stolen or destroyed, but only upon receipt of evidence of such loss, theft or destruction of such certificate, and of the ownership thereof, reasonably satisfactory to the Corporation and, in each case, customary and reasonable indemnity, if requested. Applicants for a new certificate under such circumstances shall also comply with such other reasonable regulations and procedures and pay such other reasonable third-party costs as the Corporation may prescribe.

(c) Waiver. Any waiver by the Corporation or a Holder of a breach of any provision of this Certificate of Designation shall not operate as or be construed to be a waiver of any other breach of such provision or of any breach of any other provision of this Certificate of Designation or a waiver by any other Holders. The failure of the Corporation or a Holder to insist upon strict adherence to any term of this Certificate of Designation on one or more occasions shall not be considered a waiver or deprive that party (or any other Holder) of the right thereafter to insist upon strict adherence to that term or any other term of this Certificate of Designation. Any waiver by the Corporation or a Holder must be in writing. Notwithstanding any provision in this Certificate of Designation to the contrary, any provision contained herein and any right of the Holders of Series A Preferred Stock granted hereunder may be waived as to all shares of Series A Preferred Stock (and the Holders thereof) upon the written consent of the Holders of not less than a majority of the shares of Series A Preferred Stock then outstanding, unless a higher percentage is required by the DGCL, in which case the written consent of the Holders of not less than such higher percentage shall be required.

(d) Severability. If any provision of this Certificate of Designation is invalid, illegal or unenforceable, the balance of this Certificate of Designation shall remain in effect, and if any provision is inapplicable to any Person or circumstance, it shall nevertheless remain applicable to all other Persons and circumstances. If it shall be found that any interest or other amount deemed interest due hereunder violates the applicable law governing usury, the applicable rate of interest due hereunder shall automatically be lowered to equal the maximum rate of interest permitted under applicable law.

(e) Next Business Day. Whenever any payment or other obligation hereunder shall be due on a day other than a Business Day, such payment shall be made on the next succeeding Business Day.

(f) Headings. The headings contained herein are for convenience only, do not constitute a part of this Certificate of Designation and shall not be deemed to limit or affect any of the provisions hereof.

(g) Status of Converted Series A Preferred Stock. If any shares of Series A Preferred Stock shall be converted or reacquired by the Corporation, such shares shall resume the status of authorized but unissued shares of preferred stock and shall no longer be designated as Series A Preferred Stock.

IN WITNESS WHEREOF, the undersigned has executed this Certificate of Designation this 5th day of April, 2019.

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

ANNEX A

NOTICE OF CONVERSION

(TO BE EXECUTED BY THE REGISTERED HOLDER IN ORDER
TO CONVERT SHARES OF SERIES A PREFERRED STOCK)

The undersigned Holder hereby irrevocably elects to convert the number of shares of Series A Preferred Stock indicated below, represented by stock certificate No(s). _____ (the "**Preferred Stock Certificates**"), into shares of common stock, par value $0.001 per share (the "**Common Stock**"), of Syros Pharmaceuticals, Inc., a Delaware corporation (the "**Corporation**"), as of the date written below. If securities are to be issued in the name of a person other than the undersigned, the undersigned will pay all transfer taxes payable with respect thereto. Capitalized terms utilized but not defined herein shall have the meaning ascribed to such terms in that certain Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock (the "**Certificate of Designation**") filed by the Corporation with the Secretary of State of the State of Delaware on April 5, 2019.

As of the date hereof, the number of shares of Common Stock beneficially owned by the undersigned Holder (together with such Holder's Affiliates, and any other Person whose beneficial ownership of Common Stock would be aggregated with the Holder's for purposes of Section 13(d) or Section 16 of the Exchange Act and the applicable regulations of the Commission, including any "group" of which the Holder is a member (the foregoing, "**Attribution Parties**")), including the number of shares of Common Stock issuable upon conversion of the Series A Preferred Stock subject to this Notice of Conversion, but excluding the number of shares of Common Stock which are issuable upon (A) conversion of the remaining, unconverted Series A Preferred Stock beneficially owned by such Holder or any of its Attribution Parties, and (B) exercise or conversion of the unexercised or unconverted portion of any other securities of the Corporation (including any warrants) beneficially owned by such Holder or any of its Attribution Parties that are subject to a limitation on conversion or exercise similar to the limitation contained in Section 6(c) of the Certificate of Designation, is _____ and does not exceed the Beneficial Ownership Limitation (as defined in the Certificate of Designation). For purposes hereof, beneficial ownership shall be calculated in accordance with Section 13(d) of the Exchange Act and the applicable regulations of the Commission. In addition, for purposes hereof, "group" has the meaning set forth in Section 13(d) of the Exchange Act and the applicable regulations of the Commission.

Conversion calculations:

Date to Effect Conversion:

Number of shares of Series
A Preferred Stock owned prior to Conversion:

Number of shares of Series
A Preferred Stock to be Converted:

Certificate No(s). if shares to be converted are certificated:

Number of shares of Common Stock to be
Issued:

Address for delivery of physical certificates:

or

for DWAC Delivery:

DWAC Instructions:

Broker no:

Account no:

CERTIFICATE OF AMENDMENT
OF
RESTATED CERTIFICATE OF INCORPORATION
OF
SYROS PHARMACEUTICALS, INC.

Syros Pharmaceuticals, Inc. (the "Corporation"), a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "General Corporation Law"), does hereby certify as follows:

1.The name of the Corporation is Syros Pharmaceuticals, Inc.

2.Article FOURTH of the Restated Certificate of Incorporation of the Corporation, as amended, is hereby amended by replacing the first paragraph thereof with the following:

> "FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is 710,000,000 shares, consisting of (i) 700,000,000 shares of Common Stock, $0.001 par value per share ("Common Stock") and (ii) 10,000,000 shares of Preferred Stock, $0.001 par value per share ("Preferred Stock")."

3.This Certificate of Amendment has been duly adopted by the Board of Directors and stockholders of the Corporation in accordance with Section 242 of the General Corporation Law.

[*The remainder of this page is intentionally left blank.*]

IN WITNESS WHEREOF, the Corporation has caused its duly authorized officer to execute this Certificate of Amendment on this 15th day of September, 2022.

SYROS PHARMACEUTICALS, INC.

By: /s/ Nancy Simonian

Name: Nancy Simonian, M.D.

Title: President and Chief Executive Officer

CERTIFICATE OF AMENDMENT
OF
RESTATED CERTIFICATE OF INCORPORATION
OF
SYROS PHARMACEUTICALS, INC.

Syros Pharmaceuticals, Inc. (the "Corporation"), a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "General Corporation Law"), does hereby certify as follows:

1.The name of the Corporation is Syros Pharmaceuticals, Inc.

2.Article FOURTH of the Restated Certificate of the Corporation, as amended, is hereby amended by replacing the first paragraph thereof with the following:

"FOURTH: Effective upon the filing of this Certificate of Amendment of the Restated Certificate of Incorporation with the Secretary of State of the State of Delaware (the "Effective Time"), each 10 shares of the Corporation's common stock, par value $0.001 per share (the "Common Stock"), issued and outstanding or held by the Corporation in treasury immediately prior to the Effective Time shall be reclassified and combined into one validly issued, fully paid and nonassessable share of outstanding Common Stock or treasury share, as applicable, automatically and without any action by the holder thereof upon the Effective Time and shall represent one share of Common Stock from and after the Effective Time (such reclassification and combination of shares, the "Reverse Stock Split"). The par value of the Common Stock following the Reverse Stock Split shall remain at $0.001 par value per share. No fractional shares of Common Stock shall be issued as a result of the Reverse Stock Split and, in lieu thereof, upon surrender after the Effective Time of a certificate or a book-entry position which formerly represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time, any person who would otherwise be entitled to a fractional share of Common Stock as a result of the Reverse Stock Split, following the Effective Time, shall be entitled to receive a cash payment (without interest) equal to the fraction of a share of Common Stock to which such holder would otherwise be entitled multiplied by the average (after taking into account the exact ratio of the Reverse Stock Split determined by the Board of Directors of the Corporation) of the high and low trading prices of the Common Stock on The Nasdaq Global Select Market during regular trading hours for the five trading days immediately preceding the Effective Time.

Each stock certificate or book entry position that, immediately prior to the Effective Time, represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time shall, from and after the Effective Time, automatically and without the necessity of presenting the same for exchange, represent that number of whole shares of Common Stock after the Effective Time into which the shares formerly represented by such certificate or book entry position have been reclassified (as well as the right to receive cash in lieu of fractional shares of Common Stock after the Effective Time); provided, however, that each person of record holding a certificate or book entry position that represented shares of Common Stock that were

issued and outstanding immediately prior to the Effective Time shall receive, upon surrender of such certificate or book entry position, a new certificate or book entry position evidencing and representing the number of whole shares of Common Stock after the Effective Time into which the shares of Common Stock formerly represented by such certificate or book entry position shall have been reclassified.

The total number of shares of all classes of stock which the Corporation shall have authority to issue is 80,000,000 shares, consisting of

(i) 70,000,000 shares of Common Stock, $0.001 par value per share ("Common Stock") and

(ii) 10,000,000 shares of Preferred Stock, $0.001 par value per share ("Preferred Stock")."

This Certificate of Amendment has been duly adopted by the Board of Directors and stockholders of the Corporation in accordance with the provisions of Section 242 of the General Corporation Law.

[*The remainder of this page is intentionally left blank.*]

IN WITNESS WHEREOF, the Corporation has caused its duly authorized officer to execute this Certificate of Amendment on this 16th day of September, 2022.

SYROS PHARMACEUTICALS, INC.

By: /s/ Nancy Simonian
Name: Nancy Simonian, M.D.

Title: President and Chief Executive Officer

Exhibit 10.8

SECOND AMENDMENT TO LOAN AND SECURITY AGREEMENT

THIS SECOND AMENDMENT TO LOAN AND SECURITY AGREEMENT (this "**Amendment**") is entered into as of August 31, 2022, by and among OXFORD FINANCE LLC, a Delaware limited liability company with an office located at 115 South Union Street, Suite 300, Alexandria, Virginia 22314 ("**Oxford**"), as collateral agent (in such capacity, "**Collateral Agent**"), the Lenders listed on Schedule 1.1 to the Loan Agreement (as defined below) or otherwise a party thereto from time to time including Oxford in its capacity as a Lender (each a "**Lender**" and collectively, the "**Lenders**"), and SYROS PHARMACEUTICALS, INC., a Delaware corporation with offices located at 840 Memorial Drive, Cambridge, MA 02139 ("**Borrower**").

A. Collateral Agent, Borrower and Lenders have entered into that certain Loan and Security Agreement dated as of February 12, 2020 (as amended, supplemented or otherwise modified from time to time, the "**Loan Agreement**") pursuant to which Lenders have provided to Borrower certain loans in accordance with the terms and conditions thereof;

B. Borrower has requested that Collateral Agent and the Required Lenders modify certain provisions of the Loan Agreement; and

C. Collateral Agent and the Required Lenders have agreed to amend certain provisions of the Loan Agreement, subject to, and in accordance with, the terms and conditions set forth herein, and in reliance upon the representations and warranties set forth herein.

Agreement

NOW, THEREFORE, in consideration of the promises, covenants and agreements contained herein, and other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, Borrower, the Required Lenders and Collateral Agent hereby agree as follows:

1.Definitions. Capitalized terms used but not defined in this Amendment shall have the meanings given to them in the Loan Agreement.

2.Amendments to Loan Agreement.

2.1 Section 6.10 (Financial Covenant). Section 6.10 of the Loan Agreement is amended and restated as follows:

"**6.10 MSC Investment Condition**. Borrower shall maintain unrestricted cash balance in one or more Control Accounts subject to Control Agreements in favor of Collateral Agent in an aggregate amount of not less than an amount equal to the lesser of (i) One Hundred Ten percent (110.00%) of the aggregate principal amount of outstanding Obligations (provided, however, for the period from August 1, 2022 through September 23, 2022 only, such percent during such period shall be Ninety percent (90.00%) of the aggregate principal amount of outstanding Obligations) and (ii) the amount of Borrower's and all of its Subsidiaries' (including Syros Securities) aggregate consolidated cash and Cash Equivalent assets (the "**MSC Investment Condition**")."

2.2 Compliance Certificate (Exhibit C). Exhibit C to the Loan Agreement is amended by replacing the summary of the MSC Investment Condition with the following:

"Not less than the lesser of (i) One Hundred Ten percent (110.00%) of the aggregate principal amount of outstanding Term Loans (provided, however, for the period from August 1, 2022 through September 23, 2022 only, such percent during such period shall be Ninety percent (90.00%) of the aggregate principal amount of outstanding Term Loans) and (ii) the amount of Borrower's and all of its Subsidiaries' aggregate consolidated cash and Cash Equivalent assets".

3.Limitation of Amendment.

3.1 The amendments set forth in Section 2 above are effective for the purposes set forth herein and shall be limited precisely as written and shall not be deemed to (a) be a consent to any amendment, waiver or modification of any other term or condition of any Loan Document or (b) otherwise prejudice any right, remedy or obligation which Lenders or Borrower may now have or may have in the future under or in connection with any Loan Document, as amended hereby.

3.2 This Amendment shall be construed in connection with and as part of the Loan Documents and all terms, conditions, representations, warranties, covenants and agreements set forth in the Loan Documents are hereby ratified and confirmed and shall remain in full force and effect.

4.Representations and Warranties. To induce Collateral Agent and the Required Lenders to enter into this Amendment, Borrower hereby represents and warrants to Collateral Agent and the Required Lenders as follows:

4.1 Immediately after giving effect to this Amendment (a) the representations and warranties contained in the Loan Documents are true, accurate and complete in all material respects as of the date hereof (except to the extent such representations and warranties relate to an earlier date, in which case they are true and correct in all material respects as of such date) and (b) no Event of Default has occurred and is continuing;

4.2 Borrower has the power and due authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

4.3 The organizational documents of Borrower delivered to Collateral Agent on the Effective Date, and updated pursuant to subsequent deliveries by or on behalf of the Borrower to the Collateral Agent, remain true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

4.4 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not contravene (i) any material law or regulation binding on or affecting Borrower, (ii) any material contractual restriction with a Person binding on Borrower, (iii) any order, judgment or decree of any court or other governmental or public body or authority, or subdivision thereof, binding on Borrower, or (iv) the organizational documents of Borrower;

4.5 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not require any order, consent, approval, license, authorization or validation of, or filing, recording or registration with, or exemption by any governmental or public body or authority, or subdivision thereof, binding on Borrower, except as already has been obtained or made;

4.6 This Amendment has been duly executed and delivered by Borrower and is the binding obligation of Borrower, enforceable against Borrower in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights.

5.Loan Document. Borrower, Lenders and Collateral Agent agree that this Amendment shall be a Loan Document. Except as expressly set forth herein, the Loan Agreement and the other Loan Documents shall continue in full force and effect without alteration or amendment. This Amendment and the Loan Documents represent the entire agreement about this subject matter and supersede prior negotiations or agreements.

6.Release by Borrower.

6.1 FOR GOOD AND VALUABLE CONSIDERATION, Borrower hereby forever relieves, releases, and discharges Collateral Agent and each Lender and their respective present or former employees, officers, directors, agents, representatives, attorneys, and each of them, from any and all claims, debts, liabilities, demands, obligations, promises, acts, agreements, costs and expenses, actions and causes of action, of every type, kind, nature, description

or character whatsoever, whether known or unknown, suspected or unsuspected, absolute or contingent, arising out of or in any manner whatsoever connected with or related to facts, circumstances, issues, controversies or claims existing or arising from the beginning of time through and including the date of execution of this Amendment solely to the extent such claims arise out of or are in any manner whatsoever connected with or related to the Loan Documents, the Recitals hereto, any instruments, agreements or documents executed in connection with any of the foregoing or the origination, negotiation, administration, servicing and/or enforcement of any of the foregoing (collectively "**Released Claims**").

6.2 By entering into this release, Borrower recognizes that no facts or representations are ever absolutely certain and it may hereafter discover facts in addition to or different from those which it presently knows or believes to be true, but that it is the intention of Borrower hereby to fully, finally and forever settle and release all matters, disputes and differences, known or unknown, suspected or unsuspected in relation to the Released Claims; accordingly, if Borrower should subsequently discover that any fact that it relied upon in entering into this release was untrue, or that any understanding of the facts was incorrect, Borrower shall not be entitled to set aside this release by reason thereof, regardless of any claim of mistake of fact or law or any other circumstances whatsoever. Borrower acknowledges that it is not relying upon and has not relied upon any representation or statement made by Collateral Agent or Lenders with respect to the facts underlying this release or with regard to any of such party's rights or asserted rights.

6.3 This release may be pleaded as a full and complete defense and/or as a cross-complaint or counterclaim against any action, suit, or other proceeding that may be instituted, prosecuted or attempted in breach of this release. Borrower acknowledges that the release contained herein constitutes a material inducement to Collateral Agent and the Lenders to enter into this Amendment, and that Collateral Agent and the Lenders would not have done so but for Collateral Agent's and the Lenders' expectation that such release is valid and enforceable in all events.

7.Effectiveness. This Amendment shall be deemed effective as of the date hereof upon the due execution of this Amendment by the parties thereto.

8.Counterparts. This Amendment may be executed in any number of counterparts, each of which shall be deemed an original, and all of which, taken together, shall constitute one and the same instrument. Delivery by electronic transmission (e.g. ".pdf") of an executed counterpart of this Amendment shall be effective as a manually executed counterpart signature thereof.

9.Governing Law. This Amendment and the rights and obligations of the parties hereto shall be governed by and construed in accordance with the laws of the State of New York.

[*Balance of Page Intentionally Left Blank*]

IN WITNESS WHEREOF, the parties hereto have caused this Second Amendment to Loan and Security Agreement to be executed as of the date first set forth above.

BORROWER:

SYROS PHARMACEUTICALS, INC.

By /s/ Jason Haas
Name: Jason Haas
Title: Chief Financial Officer

COLLATERAL AGENT AND LENDER:

OXFORD FINANCE LLC

By /s/ Colette H. Featherly
Name: Colette H. Featherly
Title: Senior Vice President

Exhibit 10.10

SYROS PHARMACEUTICALS, INC.

STOCK OPTION AGREEMENT

Syros Pharmaceuticals, Inc. (the "Company") hereby grants the following stock option pursuant to its 2022 Equity Incentive Plan. The terms and conditions attached hereto are also a part hereof.

Notice of Grant

Name of optionee (the "Participant"):
Grant Date:
Incentive Stock Option or Nonstatutory Stock Option:
Number of shares of the Company's Common Stock subject to this option ("Shares"):
Option exercise price per Share:
Number, if any, of Shares that vest immediately on the grant date:
Shares that are subject to vesting schedule:
Vesting Start Date:
Final Exercise Date:

Vesting Schedule:

Vesting Date:	Number of Options that Vest:

All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.

This option satisfies in full all commitments that the Company has to the Participant with respect to the issuance of stock, stock options or other equity securities.

Syros Pharmaceuticals, Inc.

___
Signature of Participant

By:
Name of Officer
Title:

___
Street Address

___
City/State/Zip Code

Syros Pharmaceuticals, Inc.

Stock Option Agreement
Incorporated Terms and Conditions

1.Grant of Option.

This agreement evidences the grant by the Company, on the grant date (the "Grant Date") set forth in the Notice of Grant that forms part of this agreement (the "Notice of Grant"), to the Participant of an option to purchase, in whole or in part, on the terms provided herein and in the Company's 2022 Equity Incentive Plan (the "Plan"), the number of Shares set forth in the Notice of Grant of common stock, $0.001 par value per share, of the Company ("Common Stock"), at the exercise price per Share set forth in the Notice of Grant. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on the Final Exercise Date set forth in the Notice of Grant (the "Final Exercise Date").

The option evidenced by this agreement is intended to be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "Code") to the maximum extent permitted by law, solely to the extent designated as an incentive stock option in the Notice of Grant. Except as otherwise indicated by the context, the term "Participant", as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2.Vesting Schedule.

This option will become exercisable ("vest") in accordance with the vesting schedule set forth in the Notice of Grant.

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3.Exercise of Option.

(a)Form of Exercise. Each election to exercise this option shall be in writing, in the form of the Stock Option Exercise Notice attached as Annex A, signed by the Participant, and received by the Company at its principal office, accompanied by this agreement, or in such other form (which may be electronic) as is approved by the Company, together with payment in full in the manner provided in the Plan. The Participant may purchase less than the number of shares covered hereby, provided that no partial exercise of this option may be for any fractional share.

(b)Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee, director or officer of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants, or advisors of which are eligible to receive option grants under the Plan (an "Eligible Participant").

(c)Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the restrictive covenants (including, without limitation, the non-competition, non-solicitation, or confidentiality provisions) of any employment contract, any non-competition, non-solicitation, confidentiality or assignment agreement to which the Participant is a party, or any other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

(d)Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for "cause" as specified in paragraph (e) below, this option shall be exercisable, within the period of one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(e)Termination for Cause. If, prior to the Final Exercise Date, the Participant's employment is terminated by the Company for Cause (as defined below), the right to exercise this option shall terminate immediately upon the effective date of such termination of employment. If, prior to the Final Exercise Date, the Participant is given notice by the Company of the termination of his or her employment by the Company for Cause, and the effective date of such employment termination is subsequent to the date of delivery of such notice, the right to exercise this option shall be suspended from the time of the delivery of such notice until the earlier of (i) such time as it is determined or otherwise agreed that the Participant's employment shall not be terminated for Cause as provided in such notice or (ii) the effective date of such termination of employment (in which case the right to exercise this option shall, pursuant to the preceding sentence, terminate upon the effective date of such termination of employment). If the Participant is subject to an individual employment agreement with the Company or eligible to participate in a Company severance plan or arrangement, in any case which agreement, plan or arrangement contains a definition of "cause" for termination of employment, "Cause" shall have the meaning ascribed to such term in such agreement, plan or arrangement. Otherwise, "Cause" shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), as determined by the Company, which determination shall be conclusive. The Participant's employment shall be considered to have been terminated for Cause if the Company determines, within 30 days after the Participant's resignation, that termination for Cause was warranted.

4.Tax Matters.

(a)Withholding. No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment of, any federal, state or local withholding taxes required by law to be withheld in respect of this option.

(b)Disqualifying Disposition. If this option is an incentive stock option and the Participant disposes of Shares acquired upon exercise of this option within two years from the Grant Date or one year after such Shares were acquired pursuant to exercise of this option, the Participant shall notify the Company in writing of such disposition.

5.Transfer Restrictions; Clawback.

(a)This option may not be sold, assigned, transferred, pledged, encumbered or otherwise disposed of by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

(b)In accepting this option, the Participant agrees to be bound by any clawback policy that the Company has in place or may adopt in the future.

6.Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

ANNEX A

Syros Pharmaceuticals, Inc.

Stock Option Exercise Notice

Syros Pharmaceuticals, Inc.
35 CambridgePark Drive, 4th Floor
Cambridge, MA 02140

Dear Sir or Madam:

I, ___ (the "Participant"), hereby irrevocably exercise the right to purchase _ shares of the Common Stock, $0.001 par value per share (the "Shares"), of Syros Pharmaceuticals, Inc. (the "Company") at $_____ per share pursuant to the Company's 2022 Equity Incentive Plan and a stock option agreement with the Company dated _ (the "Option Agreement"). Enclosed herewith is a payment of $_, the aggregate purchase price for the Shares. The certificate for the Shares should be registered in my name as it appears below or, if so indicated below, jointly in my name and the name of the person designated below, with right of survivorship.

Dated: ___

___
Signature
Print Name:

Address:
___
___

Name and address of persons in whose name the Shares are to be jointly registered (if applicable):

___

Exhibit 10.11

SYROS PHARMACEUTICALS, INC.
RESTRICTED STOCK UNIT AGREEMENT

Syros Pharmaceuticals, Inc. (the "Company") hereby grants the following restricted stock units pursuant to its 2022 Equity Incentive Plan. The terms and conditions attached hereto are also a part hereof.

Notice of Grant

Name of recipient (the "Participant"):
Grant Date:
Number of restricted stock units ("RSUs") granted:
Number, if any, of RSUs that vest immediately on the grant date:
RSUs that are subject to vesting schedule:
Vesting Start Date:

Vesting Schedule:

Vesting Date:	Number of RSUs that Vest:

All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.

This grant of RSUs satisfies in full all commitments that the Company has to the Participant with respect to the issuance of stock, stock options or other equity securities.

Syros Pharmaceuticals, Inc.

___
Signature of Participant

By:
Name of Officer
Title:

___
Street Address

___
City/State/Zip Code

Syros Pharmaceuticals, Inc.

Restricted Stock Unit Agreement
Incorporated Terms and Conditions

1.Award of Restricted Stock Units. In consideration of services rendered and to be rendered to the Company, by the Participant, the Company has granted to the Participant, subject to the terms and conditions set forth in this Restricted Stock Unit Agreement (this "Agreement") and in the Company's 2022 Equity Incentive Plan (the "Plan"), an award with respect to the number of restricted stock units (the "RSUs") set forth in the Notice of Grant that forms part of this Agreement (the "Notice of Grant"). Each RSU represents the right to receive one share of common stock, $0.001 par value per share, of the Company (the "Common Stock") upon vesting of the RSU, subject to the terms and conditions set forth herein.

1.Vesting. The RSUs shall vest in accordance with the Vesting Schedule set forth in the Notice of Grant (the "Vesting Schedule"). Any fractional shares resulting from the application of any percentages used in the Vesting Schedule shall be rounded down to the nearest whole number of RSUs. Upon the vesting of the RSU, the Company will deliver to the Participant, for each RSU that becomes vested, one share of Common Stock, subject to the payment of any taxes pursuant to Section 7. The Common Stock will be delivered to the Participant as soon as practicable following each vesting date, but in any event within 30 days of such date.

2.Forfeiture of Unvested RSUs Upon Cessation of Service. In the event that the Participant ceases to be an Eligible Participant (as defined below) for any reason or no reason, with or without cause, all of the RSUs that are unvested as of the time of such cessation shall be forfeited immediately and automatically to the Company, without the payment of any consideration to the Participant, effective as of such cessation. The Participant shall have no further rights with respect to the unvested RSUs or any Common Stock that may have been issuable with respect thereto. The Participant shall be an "Eligible Participant" if he or she is an employee, director or officer of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants or advisors of which are eligible to receive awards of RSUs under the Plan.

3.Restrictions on Transfer. The Participant shall not sell, assign, transfer, pledge, hypothecate, encumber or otherwise dispose of, by operation of law or otherwise (collectively "transfer") any RSUs, or any interest therein. The Company shall not be required to treat as the owner of any RSUs or issue any Common Stock to any transferee to whom such RSUs have been transferred in violation of any of the provisions of this Agreement.

4.Rights as a Stockholder. The Participant shall have no rights as a stockholder of the Company with respect to any shares of Common Stock that may be issuable with respect to the RSUs until the issuance of the shares of Common Stock to the Participant following the vesting of the RSUs.

5.Provisions of the Plan. This Agreement is subject to the provisions of the Plan, a copy of which is furnished to the Participant with this Agreement.

6.Tax Matters.

(a)Acknowledgments; No Section 83(b) Election. The Participant acknowledges that he or she is responsible for obtaining the advice of the Participant's own tax advisors with respect to the award of RSUs and the Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents with respect to the tax consequences relating to the RSUs. The Participant understands that the Participant (and not the Company) shall be responsible for the Participant's tax liability that may arise in connection with the acquisition, vesting and/or disposition of the RSUs. The Participant acknowledges that no election under Section 83(b) of the Internal Revenue Code of 1986, as amended, (the "Code") is available with respect to RSUs.

(a)Withholding. The Participant acknowledges and agrees that the Company has the right to deduct from payments of any kind otherwise due to the Participant any federal, state, local or other taxes of any kind required by law to be withheld with respect to the vesting of the RSUs. At such time as the Participant is not aware of any material nonpublic information about the Company or the Common Stock, the Participant shall execute the instructions set forth in Schedule A attached hereto (the "Durable Automatic Sale Instruction") as the means of satisfying such tax obligation. If the Participant does not execute the Durable Automatic Sale Instruction prior to an applicable vesting date, then the Participant agrees that if under applicable law the Participant will owe taxes at such vesting date on the portion of the award then vested the Company shall be entitled to immediate payment from the Participant of the amount of any tax required to be withheld by the Company. The Company shall not deliver any shares of Common Stock to the Participant until it is satisfied that all required withholdings have been made.

7.Miscellaneous.

(a)Section 409A. The RSUs awarded pursuant to this Agreement are intended to be exempt from or comply with the requirements of Section 409A of the Code and the Treasury Regulations issued thereunder ("Section 409A"). The delivery of shares of Common Stock on the vesting of the RSUs may not be accelerated or deferred unless permitted or required by Section 409A.

(b)Participant's Acknowledgements. The Participant acknowledges that he or she: (i) has read this Agreement; (ii) has been represented in the preparation, negotiation and execution of this Agreement by legal counsel of the Participant's own choice or has voluntarily declined to seek such counsel; (iii) understands the terms and consequences of this Agreement; (iv) is fully aware of the legal and binding effect of this Agreement; and (v) agrees that in accepting this award, he or she will be bound by any clawback policy that the Company may adopt in the future.

Schedule A

Durable Automatic Sale Instruction

This Durable Automatic Sale Instruction is being delivered to Syros Pharmaceuticals, Inc. (the "Company") by the undersigned on the date set forth below.

I hereby acknowledge that the Company has granted, or may in the future from time to time grant, to me restricted stock units ("RSUs") under the Company's equity incentive plans as in effect from time to time.

I acknowledge that upon the vesting dates applicable to any such RSUs, I will have compensation income equal to the fair market value of the shares of the Company's common stock subject to the RSU that vest on such date and that the Company is required to withhold income and employment taxes in respect of that compensation income on the applicable vesting date.

I desire to establish a process to satisfy such withholding obligation in respect of all RSUs that have been, or may in the future be, granted by the Company to me through an automatic sale of a portion of the shares of the Company's common stock that would otherwise be issued to me on each applicable vesting date, such portion to be in an amount sufficient to satisfy such withholding obligation, with the proceeds of such sale delivered to the Company in satisfaction of such withholding obligation.

I understand that the Company has arranged for the administration and execution of its equity incentive plans and the sale of securities by plan participants thereunder pursuant to an Internet-based platform administered by a third party (the "Administrator") and the Administrator's designated brokerage partner.

Upon any vesting of my RSUs from and after the date of this Durable Automatic Sale Instruction, I hereby appoint the Administrator (or any successor administrator) to automatically sell such number of shares of the Company's common stock issuable with respect to my RSUs that vest as is sufficient to generate net proceeds sufficient to satisfy the Company's minimum statutory withholding obligations with respect to the income recognized by me upon the vesting of the RSUs (based on minimum statutory withholding rates for all tax purposes, including payroll and social security taxes, that are applicable to such income), and the Company shall receive such net proceeds in satisfaction of such tax withholding obligation.

I hereby appoint the Chief Executive Officer, Chief Financial Officer, Chief Legal Officer, and the Secretary of the Company, and any of them acting alone and with full power of substitution, to serve as my attorneys in fact to arrange for the sale of shares of common stock in accordance with this Durable Automatic Sale Instruction. I agree to execute and deliver such documents, instruments and certificates as may reasonably be required in connection with the sale of the shares of common stock pursuant to this Durable Automatic Sale Instruction.

By signing below, I hereby represent to the Company that, as of the date hereof, I am not aware of any material nonpublic information about the Company or its common stock and that I am not prohibited from entering into this Durable Automatic Sale Instruction by the Company's insider trading policy or otherwise. I have structured this Durable Automatic Sale Instruction to constitute a "binding contract" relating to the sale of common stock, consistent with the affirmative defense to liability under Section 10(b) of the Securities Exchange Act of 1934 under Rule 10b5-1(c) promulgated under such Act.

_____

Participant Name: _____

Date: _____

Exhibit 10.12

SYROS PHARMACEUTICALS, INC.
RESTRICTED STOCK AGREEMENT

Syros Pharmaceuticals, Inc. (the "Company") hereby grants the following award of restricted stock pursuant to its 2022 Equity Incentive Plan. The terms and conditions attached hereto are also a part hereof.

Notice of Grant

Name of recipient (the "Participant"):
Grant Date:
Number of shares of the restricted common stock, $0.001 par value per share (the "Common Stock") awarded ("Restricted Shares"):
Vesting Start Date:

Vesting Schedule:

Vesting Date:	Number of Shares that Vest:

All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.

This restricted stock award satisfies in full all commitments that the Company has to the Participant with respect to the issuance of stock, stock options or other equity securities.

Please confirm your acceptance of this restricted stock award and of the terms and conditions of this Agreement by signing a copy of this Agreement where indicated below.

Syros Pharmaceuticals, Inc.

___
Signature of Participant

By:
Name of Officer
Title:

___
Street Address

___
City/State/Zip Code

Syros Pharmaceuticals, Inc.

Restricted Stock Agreement
Incorporated Terms and Conditions

1. Issuance of Restricted Shares.

(a) The Restricted Shares, as set forth in the Notice of Grant that forms part of this Agreement (the "Notice of Grant") are issued, subject to the terms and conditions set forth in this Restricted Stock Agreement (this "Agreement") and in the Company's 2022 Equity Incentive Plan (the "Plan") to the Participant, effective as of the grant date (the "Grant Date") as set forth on the Notice of Grant, in consideration of services rendered and to be rendered by the Participant to the Company.

(b) The Restricted Shares will be issued by the Company in book entry form only, in the name of the Participant. The Participant agrees that the Restricted Shares shall be subject to the forfeiture provisions set forth in Section 3 of this Agreement and the restrictions on transfer set forth in Section 4 of this Agreement.

2. Vesting Schedule. The Restricted Shares shall vest in accordance with the vesting schedule set forth in the Notice of Grant (the "Vesting Schedule"). Any fractional number of Restricted Shares resulting from the application of any percentages used in the Vesting Schedule shall be rounded down to the nearest whole number of Restricted Shares.

3. Forfeiture of Unvested Restricted Shares Upon Cessation of Service. In the event that the Participant ceases to be an Eligible Participant (as defined below) for any reason or no reason, with or without cause, all of the Restricted Shares that are unvested as of the time of such cessation shall be forfeited immediately and automatically to the Company, without the payment of any consideration to the Participant, effective as of such cessation. The Participant shall have no further rights with respect to any Restricted Shares that are so forfeited. The Participant shall be an "Eligible Participant" if he or she is an employee, director or officer of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants or advisors of which are eligible to receive awards of restricted stock under the Plan.

4. Restrictions on Transfer. The Participant shall not sell, assign, transfer, pledge, hypothecate, encumber or otherwise dispose of, by operation of law or otherwise (collectively "transfer") any Restricted Shares, or any interest therein, until such Restricted Shares have vested. The Company shall not be required to (i) transfer on its books any of the Restricted Shares which have been transferred in violation of any of the provisions of this Agreement or (ii) treat as owner of such Restricted Shares or to pay dividends to any transferee to whom such Restricted Shares have been transferred in violation of any of the provisions of this Agreement.

5. Restrictive Legends.

The book entry account reflecting the issuance of the Restricted Shares in the name of the Participant shall bear a legend or other notation upon substantially the following terms:

"These shares of stock are subject to forfeiture provisions and restrictions on transfer set forth in a certain Restricted Stock Agreement between the corporation and the registered owner of these shares (or his or her predecessor in interest), and such Agreement is available for inspection without charge at the office of the Secretary of the corporation."

6.Rights as a Stockholder. Except as otherwise provided in this Agreement, for so long as the Participant is the registered owner of the Restricted Shares, the Participant shall have all rights as a shareholder with respect to the Restricted Shares, whether vested or unvested, including, without limitation, rights to vote the Restricted Shares and act in respect of the Restricted Shares at any meeting of shareholders; provided that the payment of dividends on unvested Restricted Shares shall be deferred until, and shall only be paid at, such time as the shares vest.

1.Provisions of the Plan. This Agreement is subject to the provisions of the Plan, a copy of which is furnished to the Participant with this Agreement.

7.Tax Matters.

(a)Acknowledgments. The Participant acknowledges that he or she is responsible for obtaining the advice of the Participant's own tax advisors with respect to the award of the Restricted Shares and the Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents with respect to the tax consequences relating to the Restricted Shares. The Participant understands that the Participant (and not the Company) shall be responsible for the Participant's tax liability that may arise in connection with the acquisition, vesting and/or disposition of the Restricted Shares.

(b)Section 83(b) Election. The Participant understands that it may be beneficial to elect to be taxed at the time the Restricted Shares are granted by the Company rather than when and as the Restricted Shares vest by filing an election under Section 83(b) of the Internal Revenue Code of 1986, as amended, or "Section 83(b)," with the I.R.S. within 30 days from the Grant Date. The Participant acknowledges that if the Participant makes an election under Section 83(b), the Participant shall deliver written notice of such election to the Company.

THE PARTICIPANT ACKNOWLEDGES THAT IT IS SOLELY THE PARTICIPANT'S RESPONSIBILITY AND NOT THE COMPANY'S TO FILE TIMELY THE ELECTION UNDER SECTION 83(b), EVEN IF THE PARTICIPANT REQUESTS THE COMPANY OR ITS REPRESENTATIVES TO MAKE THIS FILING ON THE PARTICIPANT'S BEHALF.

(a)Withholding. The Participant acknowledges and agrees that the Company has the right to deduct from payments of any kind otherwise due to the Participant any federal, state, local or other taxes of any kind required by law to be withheld with respect to the issuance, vesting, or, if the Participant makes an election under Section 83(b), the grant of the Restricted Shares. The Participant agrees that if under applicable law the Participant will owe taxes at such vesting date on the portion of the award then vested the Company shall be entitled to immediate payment from the Participant of the amount of any tax required to be withheld by the Company.

The Company shall not remove the restrictive legend described in Section 5 hereof from any shares of Common Stock until it is satisfied that all required withholdings have been made.

8.Participant's Acknowledgments. The Participant acknowledges that he or she: (i) has read this Agreement; (ii) has been represented in the preparation, negotiation and execution of this Agreement by legal counsel of the Participant's own choice or has voluntarily declined to seek such counsel; (iii) understands the terms and consequences of this Agreement; (iv) is fully aware of the legal and binding effect of this Agreement; and (v) agrees that in accepting this award, he or she will be bound by any clawback policy that the Company may adopt in the future.

Exhibit 10.13

SYROS PHARMACEUTICALS, INC.
AMENDED AND RESTATED DIRECTOR COMPENSATION POLICY

Non-employee directors shall receive the following compensation for their service as members of the Board of Directors (the "**Board**") of Syros Pharmaceuticals, Inc. (the "**Company**").

Director Compensation

Our goal is to provide compensation for our non-employee directors in a manner that enables us to attract and retain outstanding director candidates and reflects the substantial time commitment necessary to oversee the Company's affairs. We also seek to align the interests of our directors and our stockholders and we have chosen to do so by compensating our non-employee directors with a mix of cash and equity-based compensation.

Cash Compensation

The fees that will be paid to our non-employee directors for service on the Board, and for service on each committee of the Board on which the director is then a member, and the fees that will be paid to the chair of the Board, and the chair of each committee of the Board will be as follows:

	Base	Incremental—Chair	Incremental—Non-Chair
Board of Directors	$ 40,000	$ 30,000	
Audit Committee		$ 15,000	$ 7,500
Compensation Committee		$ 10,000	$ 5,000
Research and Development Committee		$ 10,000	$ 5,000
Nominating and Corporate Governance Committee		$ 8,000	$ 4,000

The foregoing fees will be payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of such quarter that the director is not serving on our Board, on such committee or in such position.

Equity Compensation

Initial Grants. Upon initial election to our Board, each non-employee director will be granted, automatically and without the need for any further action by the Board, an initial equity award comprised of: (i) an option to purchase 12,000 shares of our common stock, which option shall have an exercise price equal to the closing trading price of the Company's common stock on the date of grant of the award, a term of ten years from the date of grant of the award, and shall vest and become exercisable as to 16.66% of the shares underlying such award on the six month anniversary of the date of grant of the award, with the remainder vesting in equal monthly installments of 2.77% of the shares underlying the initial award until the third anniversary of the date of grant of the award, and (ii) a restricted stock or restricted stock unit award (the form of such award being at the election of the director) for 8,000 shares of our common stock, which award shall vest as to 33.33% of the shares

underlying such award on each of the first three annual anniversaries of the date of grant of the award, subject in each case to the director's continued service as a director through each applicable vesting date. The vesting shall accelerate as to 100% of the shares upon a change in control of the Company.

Annual Grants. Each non-employee director who has served as a member of our Board for at least six months prior to the date of our annual meeting of stockholders for a particular year will be granted, automatically and without the need for any further action by the Board, an equity award on the date of our annual meeting of stockholders for such year comprised of: (i) an option to purchase 6,000 shares of our common stock, which option shall have an exercise price equal to the closing trading price of the Company's common stock on the date of grant of the award, a term of ten years from the date of grant of the award, and shall vest and become exercisable as to 50% of the shares underlying such award on the six month anniversary of the date of grant of the award, with the remainder vesting in equal monthly installments of 8.33% of the shares underlying the annual award until the first anniversary of the date of grant of the award, and (ii) a restricted stock or restricted stock unit award (the form of such award being at the election of the director) for 4,000 shares of our common stock, which award shall vest in its entirety on the earlier to occur of (x) the first anniversary of the date of grant of the award or (y) the date of the Company's next Annual Meeting of Stockholders, subject in each case to the director's continued service as a director through each applicable vesting date. The vesting shall accelerate as to 100% of the shares upon a change in control of the Company.

The foregoing share amounts shall be automatically adjusted in the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event effecting our common stock, or any distribution to holders of our common stock other than an ordinary cash dividend.

The initial awards and the annual awards shall be subject to the terms and conditions of our 2022 Stock Incentive Plan (the "**Plan**"), or any successor plan, and the terms of the award agreements entered into with each director in connection therewith, including without limitation the limitation on awards to non-employee directors in Section 4(b) of the Plan (or any similar provision in a successor plan).

Expenses

Upon presentation of documentation of such expenses reasonably satisfactory to the Company, each non-employee director shall be reimbursed for his or her reasonable out-of-pocket business expenses incurred in connection with attending meetings of the Board and committees thereof or in connection with other business related to the Board, and each non-employee director shall also be reimbursed for his or her reasonable out-of-pocket business expenses authorized by the Board or a committee of the Board that are incurred in connection with attendance at various conferences or meetings with management of the Company, in accordance with the Company's travel policy, as it may be in effect from time to time.

Adopted by the Board of Directors – December 19, 2019
Amended and restated by the Board of Directors – September 16, 2022

Exhibit 31.1

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

I, Nancy Simonian, certify that:

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

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

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

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

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

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

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

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

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

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

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

Syros Pharmaceuticals, Inc.

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

Dated: November 14, 2022

Exhibit 31.2

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

I, 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 14, 2022

Exhibit 32.1

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

In connection with the Quarterly Report on Form 10-Q of Syros Pharmaceuticals, Inc. (the "Company") for the quarter ended September 30, 2022 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 14, 2022

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

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

Exhibit 32.2

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

In connection with the Quarterly Report on Form 10-Q of Syros Pharmaceuticals, Inc. (the "Company") for the quarter ended September 30, 2022 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 14, 2022

/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.