UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended March 31, 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 **(State or Other Jurisdiction of Incorporation or Organization)**	**45-3772460** **(I.R.S. Employer Identification No.)**
35 CambridgePark Drive, 4th Floor **Cambridge, Massachusetts** **(Address of Principal Executive Offices)**	**02140** **(Zip Code)**

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

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

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

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

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

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

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☑	Smaller reporting company	☑
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

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

Number of shares of the registrant's common stock, $0.001 par value, outstanding on May 12, 2022: 62,819,046

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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, including our ability to enter into a non-dilutive financing arrangement to support the advancement of SY-2101 into Phase 3 clinical development;
- 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;
- conditions and events that raise doubt about our ability to continue as a going concern; 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)

	March 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 69,575	$ 92,302
Marketable securities	40,686	38,067
Contract assets	3,182	2,979
Prepaid expenses and other current assets	3,034	3,237
Total current assets	116,477	136,585
Property and equipment, net	12,554	12,844
Marketable securities - noncurrent	2,638	13,038
Other long-term assets	3,155	2,941
Restricted cash	3,086	3,086
Right-of-use asset – operating lease	13,900	14,104
Right-of-use assets – financing leases	271	337
Total assets	$ 152,081	$ 182,935
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,841	$ 3,692
Accrued expenses	13,249	15,624
Deferred revenue	7,773	10,181
Financing lease obligations, current portion	274	291
Operating lease obligation, current portion	1,789	1,720
Debt, current portion	1,667	—
Total current liabilities	27,593	31,508
Financing lease obligations, net of current portion	12	65
Operating lease obligation, net of current portion	22,378	22,858
Warrant liability	581	3,029
Debt, net of debt discount, long term	38,775	40,257
Commitments and contingencies (See Note 10)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized at March 31, 2022 and December 31, 2021; 0 shares issued and outstanding at March 31, 2022 and December 31, 2021	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at March 31, 2022 and December 31, 2021; 62,801,296 and 62,024,035 shares issued and outstanding at March 31, 2022 and December 31, 2021, respectively	61	61
Additional paid-in capital	551,679	548,815
Accumulated other comprehensive loss	(273)	(79)
Accumulated deficit	(488,725)	(463,579)
Total stockholders' equity	62,742	85,218
Total liabilities and stockholders' equity	$ 152,081	$ 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 March 31,	
	2022	2021
Revenue	$ 5,467	$ 4,827
Operating expenses:		
Research and development	25,171	20,029
General and administrative	6,949	5,739
Total operating expenses	32,120	25,768
Loss from operations	(26,653)	(20,941)
Interest income	35	10
Interest expense	(976)	(967)
Change in fair value of warrant liability	2,448	7,670
Net loss applicable to common stockholders	$ (25,146)	$ (14,228)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.40)	$ (0.23)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	63,061,423	61,379,641

See accompanying notes to unaudited condensed consolidated financial statements.

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

	Three Months Ended March 31,	
	2022	2021
Net loss	$ (25,146)	$ (14,228)
Other comprehensive loss:		
Unrealized holding loss on marketable securities	(194)	—
Comprehensive loss	$ (25,340)	$ (14,228)

See accompanying notes to unaudited condensed consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDER'S EQUITY
For the three months ended March 31, 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	56,222,746	$ 56	$ 467,518	$ —	$ (377,021)	$ 90,553
Exercise of stock options	20,134	—	157	—	—	157
Vesting of restricted stock units	206,762	—	—	—	—	—
Stock-based compensation expense	—	—	2,930	—	—	2,930
Issuance of common stock at-the-market, net of issuance costs of $5,132	5,400,000	5	70,463	—	—	70,468
Net loss	—	—	—	—	(14,228)	(14,228)
Balance at March 31, 2021	61,849,642	$ 61	$ 541,068	$ —	$ (391,249)	$ 149,880
Balance at December 31, 2021	62,024,035	$ 61	$ 548,815	$ (79)	$ (463,579)	$ 85,218
Exercise of stock options	37,700	—	1	—	—	1
Vesting of restricted stock units	739,561	—	—	—	—	—
Stock-based compensation expense	—	—	2,863	—	—	2,863
Other comprehensive loss	—	—	—	(194)	—	(194)
Net loss	—	—	—	—	(25,146)	(25,146)
Balance at March 31, 2022	62,801,296	$ 61	$ 551,679	$ (273)	$ (488,725)	$ 62,742

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

	Three Months Ended March 31,	
	2022	**2021**
Operating activities		
Net loss	$ (25,146)	$ (14,228)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	681	666
Amortization of right-of-use asset	66	65
Stock-based compensation expense	2,863	2,930
Change in fair value of warrant liability	(2,448)	(7,670)
Net amortization of premiums and discounts on marketable securities	76	—
Amortization of debt-discount and accretion of deferred debt costs	185	167
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	203	329
Accounts receivable	—	7
Contract assets	(203)	(298)
Other long-term assets	(338)	(27)
Accounts payable	(969)	63
Accrued expenses	(2,372)	(1,680)
Deferred revenue	(2,408)	(2,134)
Operating lease asset and liabilities	(207)	(180)
Net cash used in operating activities	(30,017)	(21,990)
Investing activities		
Purchases of property and equipment	(128)	(262)
Maturities of marketable securities	7,511	—
Net cash (used in) provided by investing activities	7,383	(262)
Financing activities		
Payments on financing lease obligations	(70)	(64)
Proceeds from issuance of common stock through employee benefit plans	—	157
Proceeds from the issuance of common stock through exercise of option	1	—
Proceeds from issuance of common stock and warrants in public offerings, net of issuance costs	—	70,353
Payment of issuance costs related to out of period offering	(24)	(36)
Net cash (used in) provided by financing activities	(93)	70,410
Net (decrease) increase in cash, cash equivalents and restricted cash	(22,727)	48,158
Cash, cash equivalents and restricted cash (See reconciliation in Note 6)		
Beginning of period	95,388	177,070
End of period	$ 72,661	$ 225,228
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 783	$ 789
Non-cash investing and financing activities:		
Property and equipment received but unpaid as of period end	$ 165	$ —
Offering costs incurred but unpaid as of period end	$ 10	$ 26

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 March 31, 2022, the Company had an accumulated deficit of $488.7 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.

Under ASC Topic 205-40, *Presentation of Financial Statements - Going Concern*, management is required at each reporting period to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about an entity's ability to continue as a going concern within one year after the date that the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists, management evaluates whether the mitigating effect of its plans sufficiently alleviates the substantial doubt about the Company's ability to continue as a going concern. The mitigating effect of management's plans, however, is only considered if both (i) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued and (ii) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued. Generally, to be considered probable of being effectively implemented, the plans must have been approved by the Company's board of directors before the date that the financial statements are issued.

Successful completion of the Company's development program and, ultimately, the attainment of profitable operations are dependent upon future events, including obtaining adequate financing to support the Company's cost structure and operating plan. Management's plans to alleviate its financing requirements include, among other things, pursuing one or more of the following steps to raise additional capital, none of which can be guaranteed or are entirely within the Company's control:

- raise funding through the sale of the Company's common or preferred stock;
- raise funding through debt financing; and
- establish collaborations with potential partners to advance the Company's product pipeline.

Based on its current operating plan, the Company's management believes thatits cash, cash equivalents and marketable securities of $112.9 million as of March 31, 2022 will allow the Company to meet its liquidity requirements into the second quarter of 2023. The Company's history of significant losses, its negative cash flows from operations, its limited liquidity resources currently on hand, and its dependence on its ability to obtain additional financing to fund its operations after the current resources are exhausted, about which there can be no certainty, have resulted in management's assessment that there is substantial doubt about the Company's ability to continue as a going concern for a period of at least twelve months from the issuance date of this Quarterly Report on Form 10-Q. The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business, and do not include any adjustments that may result from the outcome of this uncertainty.

If the Company is unable to raise capital when needed or on acceptable terms, or if it is unable to procure collaboration arrangements to advance its programs, the Company would be forced to discontinue some of its operations or develop and implement a plan to further extend payables, reduce overhead or scale back its current operating plan until sufficient additional capital is raised to support further operations. There can be no assurance that such a plan would be successful.

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 March 31, 2022, the results of its operations, statements of cash flows and statements of stockholders' equity for the three months ended March 31, 2022 and 2021. Such adjustments are of a normal and recurring nature. The results for the three months ended March 31, 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 Syros Pharmaceuticals, Inc. and its wholly owned subsidiaries, Syros Securities Corporation, a Massachusetts corporation formed by the Company in December 2014 to exclusively engage in buying, selling and holding securities on its own behalf, and Syros Pharmaceuticals (Ireland) Limited, an Irish limited liability company formed by the Company in January 2019. All intercompany transactions and balances have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts in the financial statements and accompanying notes. Management considers many factors in selecting appropriate financial accounting policies and in developing the estimates and assumptions that are used in the preparation of the financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, which include, but are not limited to, expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates and whether historical trends are expected to be representative of future trends. Management's estimation process may yield a range of potentially reasonable estimates and management must select an amount that falls within that range of reasonable estimates. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, estimates related to revenue recognition, warrant liability, stock-based compensation expense, accrued expenses, 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 March 31, 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 March 31, 2022, 1,000,000 Pre-Funded Warrants to purchase common stock, issued in connection with the December 2020 private placement (refer to Note 10) were included in the basic and diluted net loss per share calculation.

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

	As of March 31,	
	2022	2021
Stock options	7,527,152	6,504,401
Unvested restricted stock units	4,539,729	2,070,150
Warrants*	4,990,156	4,990,156
Total	17,057,037	13,564,707

* As of March 31, 2022 and 2021, this is comprised of 2,117,094 warrants to purchase common stock issued in connection with the Company's April 2019 financing (refer to Note 10), 27,548 warrants to purchase common stock issued in connection with the execution of the Company's loan agreement in February 2020 (refer to Note 7), 17,389 warrants to purchase common stock issued in connection with the second draw on this loan agreement in December 2020 (refer to Note 7), and 2,828,125 warrants to purchase common stock issued in connection with the private placement in December 2020 (refer to Note 10).

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. Collaboration and Research Arrangements

Collaboration with Global Blood Therapeutics

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

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

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

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

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

Either party may terminate the GBT Collaboration Agreement for the other party's uncured material breach or insolvency, and in certain other specified circumstances, subject to specified notice and cure periods. GBT may unilaterally terminate the GBT Collaboration Agreement in its entirety, for any or no reason, upon nine-months' prior written notice to the Company if such notice is delivered during the Research Term, or90 days' prior written notice to the Company if such notice is delivered after the expiration or termination of the Research Term.

GBT Collaboration Revenue

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

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

At inception, the total transaction price was determined to be approximately $60.0 million, which consisted of a $20.0 million upfront non-refundable and non-creditable technology access fee and approximately $40.0 million in reimbursable costs for employee and external research and development expenses. The GBT Collaboration Agreement also provides for development and regulatory milestones which are only payable subsequent to the exercise of the Option, and therefore are excluded from the transaction price at inception. The Company will re-evaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur. As of December 31, 2021, the Company reduced the transaction price from the initial estimate of $60.0 million to $54.2 million. The reduction of the transaction price was driven by a lower actual cost reimbursement and 2022 reimbursable cost budget approved by the Company and GBT.

During the three months ended March 31, 2022, there was no change in the total transaction price, which remained at approximately $54.2 million.

ASC 606 requires an entity to recognize revenue only when it satisfies a performance obligation by transferring a promised good or service to a customer. A good or service is considered to be transferred when the customer obtains control. As the non-exclusive research license and research and development services represent one performance obligation, the Company has determined that it will satisfy its performance obligation over a period of time as services are performed and GBT receives the benefit of the services, as the overall purpose of the arrangement is for the Company to perform the services. The Company will recognize revenue associated with the performance obligation as the research and development services are provided using an input method, according to the costs incurred as related to the research and development activities and the costs expected to be incurred in the future to satisfy the performance obligation. The transfer of control occurs during this time and is the best measure of progress towards satisfying the performance obligation.

During the three months ended March 31, 2022 and 2021, the Company recognized revenue of $5.1 million and $4.0 million, respectively, under the GBT Collaboration Agreement. As of March 31, 2022, the Company had deferred revenue outstanding under the GBT Collaboration Agreement of approximately $6.9 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 March 31, 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 months ended March 31, 2022 and 2021, the Company recognized revenue of $0.4 million and $0.8 million, respectively, under the Incyte Collaboration Agreement. As of March 31, 2022, the Company had deferred revenue outstanding under the Incyte Collaboration Agreement of approximately $0.8 million, 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 three months ended March 31, 2022 (in thousands):

	Balance at December 31, 2021	Additions	Deductions	Balance at March 31, 2022
Accounts receivable and contract assets:				
Billed receivables from collaboration partners	$ —	$ 2,857	$ (2,857)	$ —
Unbilled receivables from collaboration partners	2,979	3,181	(2,978)	3,182
Total accounts receivable and contract assets	$ 2,979	$ 6,038	$ (5,835)	$ 3,182
Contract liabilities:				
Deferred revenue - Incyte	$ 1,268	$ —	$ (421)	$ 847
Deferred revenue - GBT	8,913	—	(1,987)	6,926
Total contract liabilities	$ 10,181	$ —	$ (2,408)	$ 7,773

4. Cash, Cash Equivalents and Marketable Securities

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

Cash, cash equivalents and marketable securities consisted of the following at March 31, 2022 and December 31, 2021 (in thousands):

March 31, 2022	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash and money market funds	$ 69,575	$ —	$ —	$ 69,575
Marketable securities:				
Corporate debt securities - due in one year or less	28,915	—	(111)	28,804
US Treasury obligation - due in one year or less	12,000	—	(118)	11,882
Corporate debt securities - due in more than one year to five years	2,682	—	(44)	2,638
Total	$ 113,172	$ —	$ (273)	$ 112,899

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 three months ended March 31, 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 March 31, 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 March 31, 2022, the Company held ten securities that were in an unrealized loss position. The aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months as of March 31, 2022 was $27.4 million. There were no securities held by the Company in an unrealized loss position for more than twelve months as of March 31, 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 March 31, 2022.

5. Fair Value Measurements

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

Description	March 31, 2022	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Cash	$ 59,769	$ 59,769	—	$ —
Money market funds	9,806	9,806	—	—
Corporate debt securities - due in one year or less	28,804	—	28,804	—
US Treasury obligation - due in one year or less	11,882	11,882	—	—
Corporate debt securities - due in more than one year to five years	2,638	—	2,638	—
Total	$ 112,899	$ 81,457	$ 31,442	$ —
Liabilities:				
Warrant liability	$ 581	$ —	$ —	$ 581
Total	$ 581	$ —	$ —	$ 581

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

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

	March 31, 2022	December 31, 2021
Stock price	$ 1.19	$ 3.26
Risk-free interest rate	2.44 %	1.11 %
Dividend yield	—	—
Expected life (in years)	3.69	3.94
Expected volatility	85.49 %	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 three months ended March 31, 2022 and the year ended December 31, 2021 (in thousands):

	March 31, 2022	December 31, 2021
Fair value of warrant liability as of beginning of the period	$ 3,029	$ 19,711
Change in fair value	(2,448)	(16,682)
Fair value of warrant liability as of end of the period	$ 581	$ 3,029

6. Restricted Cash

At March 31, 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 March 31, 2022, and December 31, 2021 (in thousands):

	March 31, 2022	December 31, 2021
Cash and cash equivalents	$ 69,575	$ 92,302
Restricted cash, net of current portion	3,086	3,086
Total cash, cash equivalents and restricted cash	$ 72,661	$ 95,388

7. Oxford Finance Loan Agreement

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

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

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

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

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

The Company has the following minimum aggregate future loan payments as of March 31, 2022 (in thousands):

Nine months ending December 31, 2022	$	—
Year ending December 31, 2023		16,666
Year ending December 31, 2024		20,000
Year ending December 31, 2025		3,334
Total minimum payments	$	40,000
Less unamortized debt discount		(410)
Plus accumulated accretion of final fees		852
Total carrying value of debt		40,442
Less current portion		(1,667)
Long-term debt, net of current portion	$	38,775

For the three months ended March 31, 2022 and 2021, interest expense related to the Loan Agreement was approximately $1.0 million and $0.9 million, respectively. For the three months ended March 31, 2022, the current portion of debt is $1.7 million and the long-term portion of debt is $38.8 million as classified on the Company's condensed consolidated balance sheets as of March 31, 2022.

8. Accrued Expenses

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

	March 31, 2022	December 31, 2021
External research and preclinical development	8,521	$ 8,274
Employee compensation and benefits	3,180	6,344
Professional fees	1,495	953
Facilities and other	53	53
Accrued expenses	$ 13,249	$ 15,624

9. Commitments and Contingencies

Operating Lease

On January 8, 2019, the Company entered into a lease (the "HQ Lease") with respect to approximately52,859 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 of9.3%, 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 $1.8 million of the lease liability as short-term and $22.4 million of the lease liability as long-term as of March 31, 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 a48-month term. At the end of the term, the Company has the right to return the leased equipment, extend the lease, or buy the equipment at the then-current fair market value of the equipment. The Company accounted for the Equipment Lease as a financing lease under ASC 842 and recorded a financing lease right-of-use asset and a corresponding financing lease liability of approximately $1.0 million at the time the Equipment Lease was executed.

The following is a maturity analysis of the annual undiscounted cash flows reconciled to the carrying value of the operating and financing lease liabilities as of March 31, 2022 (in thousands):

	Operating	Financing
Nine months ending December 31, 2022	$ 2,956	$ 234
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	34,714	300
Less imputed interest	(10,547)	(14)
Total lease liability	$ 24,167	$ 286

The following table outlines the total lease cost for the Company's operating and financing leases as well as weighted average information for these leases as of March 31, 2022 (in thousands):

	Three Months Ended March 31, 2022
Lease cost:	
Operating lease cost	$ 772
Financing lease cost:	
Amortization of right-of-use asset	$ 66
Interest on lease liabilities	7
Total financing lease cost	$ 73
Cash paid for amounts included in the measurement of liabilities:	
Operating cash flows from operating lease	$ 979
Operating cash flows from financing lease	$ 78

Other information:	Three Months Ended March 31, 2022
Weighted-average remaining lease term (in years) - operating lease	7.92
Weighted-average discount rate - operating lease	9.30 %
Weighted-average remaining lease term (in years) - financing lease	1.07
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 did not incur any fees under this supply management agreement during the three months ended March 31, 2022 and 2021.

10. Stockholders' equity

Issuance of Securities through an Underwritten Public Offering

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

Issuance of Securities through a Private Placement

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

In the event of certain fundamental transactions involving the Company, the holders of Warrants may require the Company to make a payment based on a Black-Scholes valuation, using specified inputs. The holders of Pre-Funded Warrants do not have similar rights. Therefore, the Company accounted for the Warrants as liabilities, while the Pre-Funded Warrants met the permanent equity criteria classification. The Pre-Funded Warrants are classified as a component of permanent equity because they are freestanding financial instruments that are legally detachable and separately exercisable from the shares of common stock with which they were issued, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the Pre-Funded Warrants do not provide any guarantee of value or return. The initial fair value of the Warrants at issuance was $19.3 million, determined using the Black-Scholes valuation model. The Company remeasured the Warrants' fair value at March 31, 2022 and December 31, 2021 as $0.6 million and $3.0 million, respectively. The change in fair value of $2.4 million was recorded in the condensed statement of operations for the three months ended March 31, 2022.

Convertible Preferred Stock and 2019 Warrants

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

In November 2019, all 666 shares of Series A Preferred Stock were converted by the holder into666,000 shares of common stock. As of March 31, 2022, there were no shares of Series A Preferred Stock outstanding.

Each 2019 Warrant has an exercise price per share of common stock of $8.625, subject to adjustment in certain circumstances, and will expire onOctober 10, 2022. Each 2019 Warrant is immediately exercisable, provided that the holder is prohibited, subject to certain exceptions, from exercising the 2019 Warrant for shares of the Company's common stock to the extent that immediately prior to or after giving effect to such exercise, the holder, together with its affiliates and other attribution parties, would own more than 4.99% of the total number of shares of the Company's common stock then issued and outstanding. This percentage may be changed at the holders' election to a higher or lower percentage upon 61 days' notice to the Company.

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

The Series A Preferred Stock was not mandatorily redeemable and did not embody an obligation to buy back the shares outside of the Company's control in a manner that could require the transfer of assets. Additionally, the Company determined that the Series A Preferred Stock would be recorded as permanent equity, not temporary equity, given that the holders of equally and more subordinated equity would be entitled to receive the same form of consideration upon the occurrence of the event that gives rise to the redemption or events of redemption that are within the control of the Company.

Additionally, as the effective conversion price of the Series A Preferred Stock of $6.57 was below the fair value of the Company's common stock on the date of issuance of $7.50, the Company determined that the Series A Preferred Stock included a beneficial conversion feature. The Company calculated the beneficial conversion feature to be approximately $0.6 million, which was recorded as a discount to the Series A Preferred Stock at the time of issuance.

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

As of March 31, 2022, the 2019 Warrants to purchase 2,117,094 shares of common stock are outstanding and remain unexercised.

11. Stock-Based Payments

2016 Stock Incentive Plan

The 2016 Stock Incentive Plan (the "2016 Plan") was adopted by the board of directors on December 15, 2015, approved by the stockholders on June 17, 2016, and became effective on July 6, 2016 upon the closing of the Company's initial public offering ("IPO"). The 2016 Plan replaced the 2012 Equity Incentive Plan (the "2012 Plan"). Any options or awards outstanding under the 2012 Plan remained outstanding and effective. Under the 2016 Plan, the Company may grant incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards. The number of shares of the Company's common stock reserved for issuance under the 2016 Plan automatically increases on the first day of each calendar year, through the 2025 calendar year, in an amount equal to the least of (i) 1,600,000 shares of common stock, (ii) 4.0% of the outstanding shares of common stock as of such date, or (iii) such lesser amount as specified by the board of directors. This number is subject to adjustment in the event of a stock split, stock dividend or other change in the Company's capitalization. For the calendar year beginning January 1, 2022, the number of shares reserved for issuance under the 2016 Plan was increased by 1,600,000 shares. At March 31, 2022, 428,219 shares remained available for future issuance under the 2016 Plan. Under the 2016 Plan, stock options may not be granted at less than fair value on the date of grant.

2016 Employee Stock Purchase Plan

The 2016 Employee Stock Purchase Plan (the "2016 ESPP") was adopted by the board of directors on December 15, 2015, approved by the stockholders on June 17, 2016, and became effective on July 6, 2016 upon the closing of the IPO. The number of shares of the Company's common stock reserved for issuance under the 2016 ESPP automatically increases on the first day of each calendar year through the 2025 calendar year, in an amount equal to the least of (i) 1,173,333 shares of the Company's common stock, (ii) 1.0% of the total number of shares of the Company's common stock outstanding on the first day of the applicable year, and (iii) an amount determined by the Company's board of directors. For the calendar year beginning January 1, 2022, the number of shares reserved for issuance under the 2016 ESPP was increased by 620,241 shares. At March 31, 2022, 2,857,306 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 of1,110,000 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 1,000,000 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).

Stock Options

Terms of stock option agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the 2016 Plan. Stock option awards granted by the Company generally vest over four years, with 25% vesting on the first anniversary of the vesting commencement date and 75% vesting ratably, on a monthly basis, over the remaining three years. Such awards have a contractual term of ten years from the grant date.

The Company has granted certain stock options to management for which vesting accelerates upon the achievement of performance-based criteria. Milestone events are specific to the Company's corporate goals, including but not limited to certain clinical development milestones for the Company's product candidates and the Company's ability to execute on its corporate development and financing strategies. Stock-based compensation expense associated with these performance-based stock options is recognized based on the accelerated attribution model. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date. Notwithstanding any vesting in accordance with the achievement of performance-based milestones, such awards vest in full on the sixth anniversary of the vesting commencement date. As of December 31, 2020, all performance-based milestones related to these stock options were achieved. The Company did not record any additional stock-based compensation expense related to the achievement of performance-based milestones during the three months ended March 31, 2022 and 2021

The Company has granted options to purchase 75,000 shares of common stock to an advisor that vest solely upon the achievement of performance-based criteria. As of March 31, 2022, none of these performance-based criteria had been achieved. As of March 31, 2022, there was $0.3 million of unrecognized compensation cost related to this option, with a remaining contractual period of 4.5 years.

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

	Shares	Weighted Average Exercise Price	Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2021	6,657,268	$ 8.27	7.2	$ 494
Granted	951,300	1.59		
Exercised	(37,700)	0.04		
Cancelled	(43,716)	9.93		
Outstanding at March 31, 2022	7,527,152	$ 7.45	6.9	$ 26
Exercisable at March 31, 2022	4,081,501	$ 9.01	5.4	$ 26

The intrinsic value of stock options exercised during the three months ended March 31, 2022 and 2021 was $0.1 million and $0.1 million, respectively.

As of March 31, 2022, there was $12.1 million of total unrecognized compensation cost related to non-vested stock options granted to employees, which is expected to be recognized over a weighted-average period of 3.1 years.

Restricted Stock Units

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

A summary of the status of restricted stock units as of December 31, 2021 and March 31, 2022 and changes during the three months ended March 31, 2022 is presented below:

	Shares	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2021	2,687,487	$ 6.52
Granted	2,768,128	1.58
Vested	(739,561)	7.32
Forfeited	(176,325)	6.76
Outstanding at March 31, 2022	4,539,729	$ 3.37

As of March 31, 2022, there was $13.9 million of unrecognized stock-based compensation expense related to outstanding restricted stock units, with an expected recognition period of 2.9 years.

Stock-based Compensation Expense

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

	Three Months Ended March 31,			
	2022		2021	
Weighted-average risk-free interest rate	1.98	%	0.78	%
Expected dividend yield	—	%	—	%
Expected option term (in years)	6.07		6.08	
Volatility	80.70	%	82.10	%

The weighted-average grant date fair value per share of options granted in the three months ended March 31, 2022 and 2021 was $1.11 and $7.89, respectively.

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

	Three Months Ended March 31,			
	2022		2021	
Research and development	$	1,395	$	1,323
General and administrative		1,468		1,607
Total stock-based compensation expense	$	2,863	$	2,930

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, and for which evaluation is planned in combination with atezolizumab, a PD-L1 inhibitor, in BRAF-mutant colorectal cancer in a Phase 1/1b clinical trial sponsored by F. Hoffmann-La Roche AG, or Roche.

We also have multiple preclinical and discovery programs in oncology, including programs targeting the inhibition of CDK12, CDK11, and WRN. We expect that our next development candidate will be nominated from our CDK12 program in the second half of 2022.

In December 2019, we entered into a collaboration with Global Blood Therapeutics, Inc., or GBT, to discover, develop and commercialize novel therapies for sickle cell disease and beta thalassemia. We also use our gene control platform in collaboration with third parties to identify and validate targets in diseases beyond our current areas of focus. To this end, we entered into a target discovery, research collaboration and option agreement with Incyte Corporation, or Incyte, in January 2018 under which we are using our platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms.

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 both RARA-positive and RARA-negative patients, were eligible for a safety analysis. Among these patients, tamibarotene in combination with azacitidine was generally well-tolerated, with no evidence of increased toxicity relative to either as a single agent, including rates of myelosuppression that were comparable to single-agent azacitidine. As of the data cut-off, of the 18 RARA-positive patients that were evaluable for clinical response, the overall response rate, or ORR, was 67%, with a composite complete response rate of 61%, with 50% of patients achieving complete response, or CR, and 11% achieving a complete response with incomplete blood count recovery, or CRi. The median time to initial response was 1.2 months, the median duration of response was 10.8 months, and the median overall survival, or OS, among patients who achieved a CR or CRi was 18 months. As of the data cut-off, of the 28 RARA-negative patients that were evaluable for clinical response, the ORR was 43%, with a composite complete response rate of 32%, with 25% of patients achieving CR and 7% achieving CRi. The median time to initial response was 3.0 months, and the median duration of response was 10.3 months. We also presented translational data demonstrating that most RARA-positive newly diagnosed unfit AML patients 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 RARA-positive newly diagnosed HR-MDS patients, which we refer to as SELECT-MDS-1. HR-MDS is a hematologic malignancy that is closely related to AML, and as in AML, about 30% of HR-MDS patients are RARA-positive. 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 RARA-positive newly diagnosed HR-MDS patients in the double-blind placebo-controlled trial, randomized 2:1 to receive tamibarotene in combination with azacitidine or placebo with azacitidine, respectively. The primary endpoint of the trial will be the CR rate. The trial is designed with 90% power and a one-sided alpha of 0.025 to detect a difference in CR rates between the experimental and control arms. We are currently dosing patients in SELECT-MDS-1, and 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 RARA-positive newly diagnosed unfit AML patients. The trial, which we refer to as SELECT-AML-1, is designed with a single-arm safety lead-in 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 we expect to report clinical activity data from the safety lead-in portion of the trial in the second half of 2022.

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. We anticipate reporting PK and safety data from this study in mid-2022. We require additional capital to support the advancement of SY-2101 into a Phase 3 clinical trial and do not plan to pursue Phase 3 development of SY-2101 unless and until such capital is secured. We cannot provide assurance that such capital can be secured, or will be obtained on favorable terms.

SY-5609

At the European Society for Medical Oncology Congress held in September 2021, or ESMO 2021, we presented data from the dose-escalation portion of the Phase 1 multi-center, open-label study of SY-5609 evaluating patients with advanced breast, colorectal, lung, ovarian and pancreatic cancers, as well as patients with solid tumors of any histology harboring Rb pathway alterations. Patients were treated in cohorts exploring continuous daily dosing as well as intermittent dosing regimens, including seven days on treatment and seven days off, 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 have initiated an expansion cohort that includes two arms evaluating SY-5609 in combination with chemotherapy for the treatment of pancreatic cancer. Following completion of safety lead-ins, we expect to enroll approximately 50 patients with metastatic pancreatic cancer, with one arm 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 another arm exploring a SY-5609 in combination with gemcitabine and nab-paclitaxel in patients following first relapse after FOLFIRINOX. SY-5609 will be administered 7d on/7d off at a starting dose of 4 mg. in the gemcitabine combination arm, and the combination agents will be administered at the approved doses. The study will evaluate safety and tolerability, as well as efficacy measures such as disease control rate and progression free survival. We expect to report clinical activity data of SY-5609 in combination with chemotherapy from the safety lead-in portion of the trial in the second half of 2022.

Given the current financing environment, we have deprioritized our planned evaluation of SY-5609 in hematologic malignancies.

In August 2021, we announced entry into a clinical supply agreement with Roche, pursuant to which we agreed to supply SY-5609 for a combination dosing cohort with atezolizumab in Roche's ongoing Phase 1/1b INTRINSIC trial, which is evaluating multiple targeted therapies or immunotherapy, including atezolizumab, as single agents or in rational specified combinations in molecularly defined subsets of colorectal cancer patients. SY-5609 will be evaluated in combination with atezolizumab in patients with BRAF-mutant disease, and Roche plans for this arm of the trial to be open for enrollment in the first half of 2022. 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.

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 March 31, 2022 and 2021, we recognized $5.5 million and $4.8 million of revenue, of which $5.1 million and $4.0 million was related to our collaboration with GBT and $0.4 million and $0.8 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 months ended March 31, 2022 and 2021 (in thousands):

	Three Months Ended March 31,	
	2022	2021
Tamibarotene external costs	$ 6,096	$ 4,512
SY-5609 and other CDK7 program external costs	2,670	3,106
SY-2101 program external costs	1,662	767
Other research and platform program external costs	4,285	3,351
Employee-related expenses, including stock-based compensation	8,681	6,710
Facilities and other expenses	1,777	1,583
Total research and development expenses	$ 25,171	$ 20,029

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

- successful completion of preclinical studies, including activities related to preparation of investigational new drug applications, or INDs, and minimally efficacious dose studies in animals, where applicable and required, under the requirements of the U.S. Food and Drug Administration, or FDA, or another regulatory authority;
- approval of INDs for our product candidates to commence planned or future clinical trials;
- successful enrollment in, and completion of, clinical trials;
- successful data from our clinical programs that support an acceptable benefit-risk profile of our product candidates in the intended populations;
- successful development, and subsequent clearance or approval, of companion diagnostic tests for use in identifying potential patients;
- receipt of regulatory approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers for clinical supply and commercial manufacturing and, where applicable, commercial manufacturing capabilities;
- establishment and maintenance of patent and trade secret protection or regulatory exclusivity for our product candidates;
- commercial launch of our product candidates, if and when approved, whether alone or in collaboration with others;

- enforcement and defense of intellectual property rights and claims;
- maintenance of a continued acceptable safety profile of the product candidates following approval;
- retention of key research and development personnel; and
- the 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.

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 March 31, 2022 and 2021

The following table summarizes our results of operations for the three months ended March 31, 2022 and 2021, together with the changes in those items in dollars (in thousands):

	Three Months Ended March 31,			
	2022	2021	Dollar Change	% Change
Statements of Operations Data:				
Revenue	$ 5,467	$ 4,827	$ 640	13 %
Operating expenses:				
Research and development	25,171	20,029	5,142	26 %
General and administrative	6,949	5,739	1,210	21 %
Total operating expenses	32,120	25,768	6,352	25 %
Loss from operations	(26,653)	(20,941)	(5,712)	27 %
Interest income	35	10	25	250 %
Interest expense	(976)	(967)	(9)	1 %
Change in fair value of warrant liability	2,448	7,670	(5,222)	(68) %
Net loss	$ (25,146)	$ (14,228)	$ (10,918)	77 %

Revenue

For the three months ended March 31, 2022, revenue was $5.5 million, of which $5.1 million was attributable to our collaboration with GBT and $0.4 million was attributable to our collaboration with Incyte. For the three months ended March 31, 2021, revenue was $4.8 million, of which $4.0 million was attributable to our collaboration with GBT and $0.8 million was attributable to our collaboration with Incyte.

Research and Development Expense

Research and development expense increased by approximately $5.1 million, or 26%, from $20.0 million for the three months ended March 31, 2021 to $25.2 million for the three months ended March 31, 2022. The following table summarizes our research and development expenses for the three months ended March 31, 2022 and 2021, together with the changes to those items in dollars (in thousands):

	Three Months Ended March 31,			
	2022	2021	Dollar Change	% Change
External research and development	$ 13,099	$ 10,806	$ 2,293	21 %
Employee-related expenses, excluding stock-based compensation	7,286	5,386	1,900	35 %
Stock-based compensation	1,395	1,324	71	5 %
Consulting, licensing and professional fees	1,614	931	683	73 %
Facilities and other expenses	1,777	1,582	195	12 %
Total research and development expenses	$ 25,171	$ 20,029	$ 5,142	26 %

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

- an increase of approximately $2.3 million, or 21%, for external research and development costs, primarily due toincreases in costs associated with the continued advancement of our existing clinical trials of tamibarotene, SY-2101 and SY-5609, and advancement of our preclinical programs, including our sickle cell disease development activities in collaboration with GBT;

- an increase of approximately $1.9 million, or 35%, for employee-related expenses, including increased salary and benefits, primarily due to our increased headcount;

- an increase of approximately $0.7 million, or 74%, for consulting, licensing and professional fees, primarily related to the advancement of our clinical and pre-clinical programs; and
- an increase of approximately $0.2 million, or 12%, for facilities and other expenses, primarily due to our increased headcount.

General and Administrative Expense

General and administrative expense increased by approximately $1.2 million, or 21%, from $5.7 million for the three months ended March 31, 2021 to $6.9 million for the three months ended March 31, 2022. The change in general and administrative expense was primarily attributable to an increase in employee-related expenses driven by increased headcount, an increase in legal costs including patent prosecution expenses, and an increase in consulting fees.

Interest Income

Interest income was derived generally from our investments in cash, cash equivalents, and marketable securities. The increase in interest income during the three months ended March 31, 2022 as compared to the three months ended March 31, 2021 was due to an increase in our investments in these securities during the period ended March 31, 2022.

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 March 31, 2021 to the three months ended March 31, 2022. The increase in interest expense during the three months ended March 31, 2022 as compared to the three months ended March 31, 2021 was driven by a higher average outstanding credit facility balance during the three months ended March 31, 2022.

Change in Fair Value of Warrant Liability

The change in fair value of warrant liability during the three months ended March 31, 2022 as compared to the three months ended March 31, 2021 was a result of the remeasurement of the fair value of warrants issued in connection with the December 2020 private placement.

Liquidity and Capital Resources

Sources of Liquidity

We funded our operations from inception through March 31, 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 February 12, 2020, we entered into a Loan and Security Agreement, or the Loan Agreement, with Oxford. Pursuant to the Loan Agreement, a term loan of up to an aggregate principal amount of $60.0 million is available to us. A $20.0 million term loan was funded on February 12, 2020, and another $20.0 million term loan was funded on December 23, 2020. As of March 31, 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 March 31, 2022, $75.0 million in common stock remained available for future issuance under the sales agreement.

As of March 31, 2022, $224.4 million of securities remained available for future issuance under the shelf registration statement.

As of March 31, 2022, we had cash, cash equivalents, and marketable securities of approximately $112.9 million.

Cash Flows

The following table provides information regarding our cash flows for the three months ended March 31, 2022 and 2021 (in thousands):

	Three Months Ended March 31,	
	2022	2021
Net cash (used in) provided by:		
Operating activities	$ (30,017)	$ (21,990)
Investing activities	7,383	(262)
Financing activities	(93)	70,410
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (22,727)	$ 48,158

Net Cash Used in Operating Activities

Net cash used in operating activities for the three months ended March 31, 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 $30.0 million during the three months ended March 31, 2022 compared to $22.0 million for the three months ended March 31, 2021. The increase in net cash used in operating activities during the three months ended March 31, 2022 was primarily due to $5.9 million increase in loss from operations and $2.1 million increase in net operating assets during the three months ended March 31, 2022.

Net Cash Provided by (Used in) Investing Activities

Net cash provided by investing activities was $7.4 million during the three months ended March 31, 2022 compared to net cash used in investing activities of $0.3 million during the three months ended March 31, 2021. The increase in net cash provided by investing activities was primarily due to maturities of marketable securities of $7.5 million, offset by the purchase of $0.1 million of property and equipment during the three months ended March 31, 2022, as compared to the decrease in net cash used in investing activities due to the $0.3 million purchase of property and equipment during the three months ended March 31, 2021.

Net Cash (Used in) Provided by Financing Activities

Net cash used in financing activities was $0.1 million during the three months ended March 31, 2022 compared to net cash provided by financing activities of $70.4 million for the three months ended March 31, 2021. Cash used in financing activities for the three months ended March 31, 2022 was primarily due to $0.1 million of payments made under our financing lease. In comparison, the cash provided by financing activities for the three months ended March 31, 2021 was primarily due to net proceeds of $70.4 million from a public offering of shares of our common stock, and $0.2 million of proceeds from the exercise of stock options, offset by $0.1 million of payments made under our financing lease.

Funding Requirements and Going Concern

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.

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 oftamibarotene, SY-2101 and SY-5609 and any associated companion diagnostic tests;
- research and preclinical development efforts for any future product candidates that we may develop;
- the number of future product candidates that we pursue and their development requirements;
- our ability to enter into, and the terms and timing of, any collaborations, licensing agreements or other arrangements;
- whether a drug candidate will be nominated to enter investigational new drug application-enabling studies under our sickle cell disease collaboration with GBT, whether GBT will exercise its option to exclusively license intellectual property arising from the collaboration, whether and when any option exercise fees, milestone payments or royalties under the collaboration agreement with GBT will ever be paid, and whether we exercise our U.S. co-promotion option under the GBT agreement;
- whether our target discovery collaboration with Incyte will yield any validated targets, whether Incyte will exercise any of its options to exclusively license intellectual property directed to such targets, and whether and when any of the target validation fees, option exercise fees, milestone payments or royalties under the collaboration agreement with Incyte will ever be paid;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the costs of acquiring potential new product candidates or technology;
- the costs of any physician education programs relating to selecting and treating genomically defined patient populations;
- the timing and amount of milestone and other payments due to licensors for patent and technology rights used in our gene control platform or to TMRC Co. Ltd., or TMRC, associated with the development, manufacture and commercialization of tamibarotene;
- the timing and amount of milestone payments due to Orsenix associated with the development and commercialization of SY-2101;
- revenue received from commercial sales, if any, of our current and future product candidates;
- our headcount growth and associated costs as we advance our research and development programs and establish a commercial infrastructure;

- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the 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.

We have incurred significant net operating losses in every year since our inception. We expect to continue to incur significant and increasing net operating losses for at least the next several years. Our net losses were $86.6 million, $84.0 million and $75.4 million for the years ended December 31, 2021, 2020 and 2019, respectively. As of March 31, 2022, we had an accumulated deficit of $488.7 million. We have not generated any revenues from product sales, have not completed the development of any product candidate and may never have a product candidate approved for commercialization. We have financed our operations to date primarily through a credit facility, the sale of equity securities and through license and collaboration agreements. We have devoted substantially all of our financial resources and efforts to research and development and general and administrative expense to support such research and development. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

As discussed in Note 1 of the Notes to the Condensed Consolidated Financial Statements on Form 10-Q, under ASC Topic 205-40, *Presentation of Financial Statements - Going Concern*, management is required at each reporting period to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about an entity's ability to continue as a going concern within one year after the date that the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued.

Based on our current operating plan, we anticipate that our cash, cash equivalents and marketable securities of $112.9 million as of March 31, 2022 will allow us to meet our liquidity requirements into the second quarter of 2023. Our history of significant losses, our negative cash flows from operations, our limited liquidity resources currently on hand, and our dependence on its ability to obtain additional financing to fund our operations after the current resources are exhausted, about which there can be no certainty, have resulted in our assessment that there is substantial doubt about our ability to continue as a going concern for a period of at least twelve months from the issuance date of this Quarterly Report on Form 10-Q. We have plans in place to mitigate this risk, which primarily consist of raising additional capital through a combination of equity or debt financings and potential new collaborations and reducing cash expenditures. To this end, we plan to seek sources of non-dilutive financing to support the advancement of SY-2101 into a Phase 3 clinical trial and do not plan to pursue Phase 3 development of SY-2101 unless and until such financing is obtained. In addition, we have elected to deprioritize our planned evaluation of SY-5609 in patients with hematologic malignancies. There is no guarantee that we will be successful in our capital raising efforts or that we will be unable to continue our other research and development programs as planned.

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 March 31, 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 three-month periods ended March 31, 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 March 31, 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 fundingto execute our operating plan and continue to operate as a going concern, 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 March 31, 2022 will enable us to fund our planned operating expense and capital expenditure requirements into the second quarter of 2023. These funds may not be sufficient to fund operations for at least the next twelve months from the date of issuance of these consolidated financial statements which raises substantial doubt about our ability to continue as a going concern. Our future viability beyond one year from the date of issuance of these consolidated financial statements is dependent on our ability to raise additional capital to finance our operations. 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. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Although management plans to pursue additional funding, there is no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us to fund continuing operations, or at all.

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 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 platformor to TMRC Co. Ltd., or TMRC, associated with the development, manufacture and commercialization oftamibarotene;
- 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 increase 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 Finance LLC, or Oxford, that we entered into in February 2020, 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 do not plan to pursue Phase 3 development of SY-2101 unless and until we secure additional capital. We cannot provide assurance that such capital 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 recently announced that we do not plan to pursue Phase 3 development of SY-2101 unless and until we secure additional capital. In addition, we have elected to deprioritize our planned evaluation of SY-5609 in patients with hematologic malignancies.

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.

Risks Related to Our Intellectual Property

We may not be able to enforce our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and other countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop and market their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Further, a decree was adopted by the Russian government in March 2022 allowing Russian companies and individuals to exploit inventions owned by patent holders from the United States without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia.

Agreements through which we license patent rights may not give us sufficient rights to permit us to pursue enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents (or control of enforcement or defense) of such patent rights in all relevant jurisdictions as requirements may vary.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Moreover, such proceedings could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

Item 6. Exhibits.

Exhibit No.	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant, including the Certificate of Designation of Preferences, Rights and Limitation of Series A Convertible Preferred Stock of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2019 (File No. 001-37813) filed on May 1, 2019).
3.2	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).
10.1*	Master Collaboration Agreement dated March 7, 2022 between Syros Pharmaceuticals, Inc. and QIAGEN Manchester Limited. 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)

* Portions of this exhibit have been omitted pursuant to Item 601 of Regulation S-K promulgated under the Securities Act of 1933, as amended, because the information is not material and is a type of information that the registrant treats as private or confidential.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Syros Pharmaceuticals, Inc.

Date: May 16, 2022

By: /s/ Jason Haas

Jason Haas

Chief Financial Officer (Principal Financial Officer)

Exhibit 10.1

CONFIDENTIAL

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

MASTER COLLABORATION AGREEMENT

for Companion Diagnostics

Between Syros Pharmaceuticals, Inc.
35 CambridgePark Drive

Cambridge, MA 02140
hereinafter **"SYROS"**

and QIAGEN Manchester Limited
Skelton House, Lloyd Street North
Manchester, M15 6SH,
England
hereinafter **"QIAGEN"**

dated: March 7, 2022 ("Effective Date")

WHEREAS,

SYROS is a biopharmaceutical company engaged in the research and development of products for the treatment of human disease and conditions, including cancer;

QIAGEN is a global biotechnology company engaged in the research, development, manufacture and commercialization of diagnostic products, including companion diagnostics to aid in the selection and use of pharmaceutical products;

QIAGEN and SYROS wish to establish a legal framework for continued collaborations relating to QIAGEN's development and commercialization of a companion diagnostic product for use with SYROS' pharmaceutical products.

NOW, therefore, the Parties agree as follows:

1. Definitions.

1.1. The following terms used in the Agreement shall have the meanings set forth below:

"**Activities**" shall mean the activities set forth in a Schedule to this Agreement to be performed by each Party in connection with a particular Project for SYROS.

"**Affiliate**" shall mean any entity which, directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with a Party, as the case may be. As used in this definition, "control" shall mean the possession of the power to direct or cause the direction of the management and policies of an entity, whether through the ownership of the outstanding voting securities or by contract or otherwise.

"Agreement" shall mean this Master Collaboration Agreement and any Schedules executed hereunder.

"Analytical Performance Data" shall mean all [**] related to the analytical performance of the QIAGEN IVD under the Project as generated by or on behalf of either Party or both Parties during the course of performing the Activities under a Schedule, which includes but is not limited to: data to support development and optimization of the QIAGEN IVD, data to support the limit of detection, limit of blank, accuracy, cross reactivity, reproducibility and stability of the QIAGEN IVD, excluding any Clinical Data and Biomarker Data.

"Applicable Law" shall mean any country, federal, state, provincial, commonwealth, cantonal or local government law, directive, statute, rule, requirement, code, regulation, permit, ordinance, authorization or similar such governmental requirement and interpretation and guidance documents of the same by a Governmental Authority or any industry self-regulatory principles, in each case, that are applicable to one or more of QIAGEN, SYROS, this Agreement or the Activities, as the context requires.

"**Background Intellectual Property**" shall mean, with respect to a Party, all Intellectual Property that (i) is in existence and Controlled by such Party at the Effective Date, (ii) becomes Controlled by such Party after the Effective Date and is not Foreground Intellectual Property, or (iii) is obtained by a Party pursuant to Section 9.6.

"Biomarker" shall mean one or more specific genes, genetic sequences, proteins or other defined characteristic, including defined characteristics identified by software algorithms, that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or responses, including pharmacologic responses, to an exposure or intervention including

therapeutic intervention. With respect to a Project, "Biomarker" shall be further defined and described in the Schedule for such Project.

"Biomarker Data" shall mean all Project Data relating to the Biomarkers, all as generated by or on behalf of either or both Parties during the course of performing Activities under a Project or Schedule.

"**Business Day**" means any day other than a Saturday, Sunday, bank holiday, or public holiday in the United States or the United Kingdom.

"Clinical Data" shall mean all [**] relating to patients or subjects in connection with a Clinical Trial, including Project Data relating to patient populations, therapy and therapeutic efficacy, clinical outcome data (*i.e,*, any data related to the performance of the SYROS Product (e.g., safety, toxicity, etc.)), all as generated by or on behalf of either or both Parties during the course of performing Activities under a Project or Schedule.

"**Clinical Trial**" shall mean a clinical investigation of a SYROS Product undertaken or supported by SYROS, alone or with a third party, as part of the development of such pharmaceutical product to obtain information relating to patient outcome and/or selection for therapy with such pharmaceutical product, which clinical investigation includes the use of the QIAGEN IVD or any prototype of it developed in the respective Project. For clarification, a Clinical Trial under this definition may include a bridging study or other clinical performance study.

"**Clinical Trial Assay**" shall mean an investigational use only device which is developed by QIAGEN under this Agreement solely for use in Clinical Trials.

"**Commercialization**" and "**Commercialize**" shall refer to all activities (including Activities) undertaken relating to the pre-marketing, marketing, distribution, manufacture (or having manufactured), importing/exporting, offering for sale, seeking pricing and reimbursement approval, sale and support of a SYROS Product or QIAGEN IVD. For clarification, this excludes Activities under Development Projects.

"Commercially Reasonable Efforts" shall mean with respect to any obligations of a Party under this Agreement, such efforts and resources substantially equivalent [**], in each case as [**], and in no event less than reasonable, good faith efforts, it being understood that the fact that [**], shall be taken into account when considering [**].

"**Competing QIAGEN Test**" means (a) an assay, developed and/or Commercialized by or on behalf of QIAGEN or its Affiliates or any third party, regardless of the diagnostic instrumentation or device, firmware base software and user interface software used therefore (b) that is capable of [**].

"**Confidential Information**" shall mean all information and materials provided by one Party or its Representatives (the "**Disclosing Party**") to the other Party or its Representatives (the "**Receiving Party**") during the Term of this Agreement and designated as confidential by the Disclosing Party when provided or which would reasonably be understood to be confidential based on the nature of the information or the circumstances of disclosure. Notwithstanding the foregoing, or any other term or condition of this Agreement: (a) the SYROS Foreground IP, the Material, Biomarker Data and the Clinical Data shall each be deemed the Confidential Information of SYROS, and SYROS shall be deemed the Disclosing Party with respect thereto, regardless of which party generates or discloses such information; and (b) the QIAGEN Foreground IP, the QIAGEN IVD System and the Analytical Performance Data shall each be deemed the Confidential Information of QIAGEN, and QIAGEN shall be deemed the Disclosing Party with respect thereto, regardless of which party generates or discloses such information. The specific terms and conditions of this Agreement are Confidential Information of both Parties, and both Parties shall be deemed to be the Disclosing Party with respect thereto, but the existence of the Agreement is not Confidential Information.

"Contract Laboratory" shall have the meaning given it in Section 5.2.

"Control" or "Controlled" or "Controlling" shall mean, with respect to any item of Intellectual Property, the possession of the right, whether directly or indirectly, and whether by ownership, license or otherwise, to assign, or to grant the other Party access or a license or sublicense to such Intellectual Property, as applicable, without violating the terms of any agreement or other arrangement with a third party.

"**Deliverables**" shall mean the Project Data, and documents, filings and/or other materials to be provided to SYROS by QIAGEN in connection with a particular Project, as specified in a Schedule.

"Development Project" shall mean a project performed under this Agreement, as agreed between the Parties and set out in a Schedule. Development Projects may include (i) biomarker identification and validation, (ii) prototype assay development, (iii) companion diagnostic proof of concept, (iv) *in vitro* diagnostic development, (v) enrolment assay development, (vi) Clinical Trial support and regulatory consultation, (vii) support of a Regulatory Submission for a SYROS Product; and/or (viii) Regulatory Submission and QIAGEN IVD registration; which project ultimately may result in the creation and Commercialization of a QIAGEN IVD in Markets for a SYROS Product under this Agreement.

"**FDA**" shall mean the United States Food and Drug Administration and any successor agency.

"**Foreground Intellectual Property**" shall mean any and all Intellectual Property arising directly from work performed under a Project under this Agreement, whether conceived, discovered, reduced to practice or writing, generated or developed by or on behalf of SYROS or its Affiliates or by its Representatives, and/or by or on behalf of QIAGEN or its Affiliates or by its Representatives, solely or jointly.

"**Governmental Authority**" shall mean any court, agency, authority, department, regulatory body or other instrumentality of any government or country or of any national, federal, state, provincial, regional, county, city or other political subdivision of any such government or any supranational organization of which any such country is a member.

"**Intellectual Property**" shall mean all inventions, know-how and other intellectual property, including tangible material, or its intangible equivalent in unwritten or oral form, and all patent rights (pending or issued), copyright, trademark, trade secret and other proprietary rights, excluding Project Data.

"**IVD**" shall mean *in vitro* diagnostic medical device as defined in the US Code of Federal Regulations Title 21, Section 809.3 or the Regulation (EU) 2017/746 of the European Parliament, the European directive 98/79/EC, or any similar definitions set by Governmental Authorities in markets outside of the United States and the European Union. For the avoidance of doubt, the term IVD includes companion diagnostics for a pharmaceutical product as defined in FDA's "Guidance for Industry and Food and Drug Administration Staff – In Vitro Companion Diagnostic Devices" (August 6, 2014).

"Joint Foreground IP" shall mean all Foreground Intellectual Property that is not QIAGEN Foreground IP or SYROS Foreground IP.

"**Markets**" shall mean the countries and territories of the world in which the Parties mutually agree to jointly Commercialize (or have Commercialized) the SYROS Product and the QIAGEN IVD, as specified in a Schedule.

"**Materials**" shall mean the biological samples, compounds, reagents, supplies, products and other goods that SYROS delivers or causes one or more third parties to deliver to QIAGEN, or QIAGEN procures from a third party at SYROS' cost, for purposes of performing this Agreement.

"**Party**" shall mean SYROS or QIAGEN as the context requires and "**Parties**" shall mean both SYROS and QIAGEN.

"**PMA**" shall mean Pre-Market Approval as defined by FDA.

"**Project**" shall mean a Development Project performed under this Agreement and/or subsequent Commercialization of the respective QIAGEN IVD.

"Project Data" shall mean (i) information, data, results and reports generated from work performed under this Agreement and (ii) experimental procedures, analysis and protocols utilized in the performance of a Project, in either case by or on behalf of SYROS or its Affiliates or Representatives, or by or on behalf of QIAGEN or its Affiliates or Representatives, solely or jointly, and all copyright, trade secret and other propriety rights therein. For the avoidance of doubt, Project Data shall not include information regarding QIAGEN's manufacturing or quality management processes, protocols or systems.

"Project-Related Background IP" shall mean (a) in the case of SYROS, Background Intellectual Property Controlled by Syros or any of its Affiliates that relates to the SYROS Product (as identified in a Schedule), Material or any SYROS Biomarker, or any use or other exploitation thereof, and (b) in the case of QIAGEN, Background Intellectual Property Controlled by QIAGEN or any of its Affiliates that relates to the QIAGEN IVD System, the QIAGEN IVD, or any QIAGEN Biomarker or any use or other exploitation thereof.

"QIAGEN Biomarker" shall mean Biomarkers which are part of QIAGEN Background Intellectual Property and identified in a Schedule.

"**QIAGEN Biomarker Data**" is defined as [**].

"QIAGEN Domain Names" shall mean any Domain Name identical or similar with the QIAGEN Trademarks under any ccTLD (country code Top Level Domain) and gTLD (generic Top Level Domain) address area.

"QIAGEN Foreground IP" shall mean any and all Foreground Intellectual Property that [**].

"QIAGEN IVD" shall mean an IVD developed by QIAGEN in the course of a Project including its respective development stages.

"QIAGEN IVD System" shall mean a diagnostic instrumentation or device, firmware base software and user interface software, and associated reagents, including those for sample preparation, which may include, for example, the RGQ instrument.

"QIAGEN Trademarks" shall mean the trademarks which QIAGEN uses for the Commercialization of the QIAGEN IVD to be used in connection with a SYROS Product.

"**Regulatory Approval**" means, with respect to a regulatory jurisdiction, any and all licenses, permits, registrations or authorizations, clearances and approvals of (including, if required for sale in any country, pricing approval), and all registrations, filings and other notifications to, any Governmental Authority (including applications therefor) necessary for the development, testing,

manufacture, production, distribution, marketing, sale or use of an in vitro assay or a drug product in such regulatory jurisdiction in accordance with Applicable Law. With regard to an IVD, Regulatory Approval would occur upon FDA approval of a Premarket Approval (PMA) for the IVD and similar approvals of Governmental Authorities in other jurisdictions for marketing authorization as an IVD.

"Regulatory Submission" shall mean with respect to a regulatory jurisdiction, any and all submissions, which are necessary to obtain and maintain a Regulatory Approval.

"Representatives" shall mean with respect to each Party, such Party's directors, officers, employees, consultants, and agents, and those of its Affiliates and subcontractors (including Contract Laboratories) who contribute to the performance of a Project.

"Schedule" shall mean an individual agreement executed by the Parties for the performance of a Project, as further described in Article 3 of this Agreement.

"SYROS Biomarker" shall mean Biomarkers which are part of SYROS Background Intellectual Property and identified in a Schedule.

"**SYROS Biomarker Data**," is defined as [**].

"SYROS Domain Names" shall mean any Domain Name identical or similar with the SYROS Trademarks under any ccTLD (country code Top Level Domain) and gTLD (generic Top Level Domain) address area.

"**SYROS Foreground IP**" shall mean any and all Foreground Intellectual Property that [**].

"**SYROS Product**" shall mean any biological or chemical substance identified in a Schedule that SYROS is developing or Commercializing for the prevention, treatment, or cure of a disease, syndrome or condition in human beings or animals.

"SYROS Trademarks" shall mean the trademarks which SYROS uses for the Commercialization of the SYROS Product with which a QIAGEN IVD will be used in connection with such SYROS Product.

"Trademark" shall mean the SYROS Trademarks and the QIAGEN Trademarks.

1.2. Other Definitional and Interpretative Provisions. The words "hereof", "herein" and "hereunder" and words of like import used in this Agreement shall refer to this Agreement as a whole and not to any particular provision of this Agreement. The captions herein are included for convenience of reference only and shall be ignored in the construction or interpretation hereof. Any capitalized term used in

any Schedule but not otherwise defined therein shall have the meaning as defined in this Agreement. Any singular term in this Agreement shall be deemed to include the plural, and any plural term the singular. Whenever the words “include”, “includes” or “including” are used in this Agreement, they shall be deemed to be followed by the words “without limitation”, whether or not they are in fact followed by those words or words of like import. This Agreement will be fairly interpreted in accordance with its terms and without any strict construction in favor of or against either Party.

2. **Term**. This Agreement shall commence on the Effective Date and continue for an initial term of the later of: (a) five (5) years; (b) expiration or termination of all Schedules executed hereunder or (c) termination of this Agreement pursuant to Section 15 (“Initial Term”). Thereafter, this Agreement shall automatically renew for additional periods of one (1) year each (together with the Initial Term, the “Term”).

3. **Projects.**

3.1. Exclusivity.

(a) Non-Exclusive Nature. The Parties agree that the nature of the relationship under the Agreement is non-exclusive.

(b) Development. Notwithstanding Section 3.1(a), the Parties may agree in a Schedule that, for a specified time period and/or disease indication as set forth in the Schedule, neither QIAGEN nor its Affiliates will develop, acquire, license, manufacture or distribute for itself, or enter into any agreement or relationship with a third party to develop, acquire, license, manufacture or distribute any Competing QIAGEN Test. Any such agreement by QIAGEN in a Schedule shall be subject to good faith negotiation of compensation to QIAGEN for the foregoing restriction.

3.2. Schedules. The Schedule for the Activities to be conducted under the initial Project is attached hereto as Appendix 1, which shall be considered Schedule No. 1. For each additional Project to be conducted under this Agreement, the Parties shall negotiate and execute a Schedule using the format provided in Appendix 1. Once executed by both Parties, the Schedule and any subsequent amendment(s) thereto shall be governed by the terms of this Agreement . With respect to Development Projects, QIAGEN shall use Commercially Reasonable Efforts to perform the Activities and provide the Deliverables as set forth in the relevant Schedule and this Agreement, including adherence to all Applicable Law, any additional requirements set forth in a Schedule and the terms of this Agreement. QIAGEN shall comply with all reasonable and applicable guidelines

and instructions that SYROS provides in writing regarding the use, storage or handling of Materials, patient samples or the SYROS Product. QIAGEN shall be responsible for the quality, technical accuracy and completeness of all Deliverables to be generated or provided by it under this Agreement or a Schedule. QIAGEN shall be responsible for the professional quality, training and supervision of all of its, its Affiliates' and permitted subcontractors' personnel who are engaged in the performance of any Activities for a Project under a Schedule. QIAGEN will perform its foregoing obligations in good faith, using Commercially Reasonable Efforts to meet the milestones set forth in each Schedule.

3.3. Scope Changes. In the event the Parties agree that the Activities or Deliverables of a Project should be modified, or that additional Activities or Deliverables should be conducted or provided, the Parties shall prepare a written amendment of the Schedule for execution by the Parties. A Party shall not vary from the Activities and Deliverables set out in the original Schedule until the Parties have executed a written amendment to the relevant Schedule. Notwithstanding the foregoing, in the event that a circumstance arises which was not reasonably anticipated by the Parties and which renders a Party's ability to perform certain Activities or Deliverables technically or scientifically impossible or impracticable, the Parties shall negotiate a scope change amendment in good faith for a period of [**]. In the event the Parties are unable to agree upon such scope change amendment in these circumstances, either Party shall have the right to terminate the applicable Schedule upon written notice to the other Party.

3.4. Conflicting Provisions. In the event there is a specific conflict between the terms or conditions of this Agreement and the terms or conditions of any Schedule, the terms and conditions of this Agreement shall govern, unless the Schedule specifically and expressly supersedes this Agreement on a specific matter and then only with respect to the particular Schedule and the matter so specified.

4. Materials and Records

4.1. Materials Delivery. Materials required for the conduct of the Project shall be outlined in the Schedule or otherwise agreed in writing by the Parties. As between SYROS and QIAGEN, SYROS shall retain all right, title and interest in and to Materials, and QIAGEN shall retain all right, title and interest in and to any other materials used in the Project which were provided or procured by or on behalf of QIAGEN at QIAGEN's expense to the extent not included in a

Deliverable provided under a Schedule. SYROS shall ensure that any Materials are de-identified of personal health information prior to shipment to QIAGEN. SYROS acknowledges that the provision of Materials by SYROS and third parties on behalf of SYROS is largely beyond the control of QIAGEN, and therefore QIAGEN shall not be held liable for delays to the Project to the extent caused by late shipments of Materials or defective Materials to be provided by or on behalf of SYROS, where the delay was not caused by QIAGEN. For purposes of clarity, each Party shall use Commercially Reasonable Efforts to ensure the timely and sufficient supply of Materials to be provided or procured by such Party pursuant to a Schedule, including ordering Materials to be procured by such Party from a third party provider within such provider's ordering lead times.

4.2. Use Restrictions. QIAGEN shall use and handle the Materials in accordance with any applicable documentation, reasonable handling procedures for similar materials, applicable common scientific standards of care, Applicable Law, and SYROS's written instructions provided to QIAGEN, and upon receipt of the Materials, shall be responsible for the chain of custody of the Materials. In no event shall QIAGEN use the Materials for any purpose other than the Activities described in the applicable Schedule. None of the Materials shall be transferred or sold by QIAGEN to third parties except to subcontractors approved by SYROS in accordance with the terms of this Agreement and who require access to the SYROS Materials to perform the Activities. QIAGEN shall not use the Materials for testing in or treatment of human subjects except if and to the extent expressly described in the applicable Schedule. QIAGEN understands and agrees that the Materials are experimental in nature and that SYROS shall not be liable for any loss, claim, damage or liability which may arise from the use, storage or handling of the Materials by QIAGEN . Unless otherwise set forth in the applicable Schedule, upon SYROS' written request and at SYROS' expense, QIAGEN shall, at SYROS' option, deliver to SYROS or destroy (in which case such destruction shall be certified to SYROS in writing) all Materials provided by SYROS in QIAGEN's possession or control.

4.3. Records Retention. QIAGEN shall retain all Project Data (including all records related thereto) generated during the performance of the Activities, separately from any records and data generated during performance of activities for clients other than SYROS, for a period of not less than [**], or for such longer period as required by Applicable Law, in a form appropriate for regulatory and intellectual property purposes. Upon written request from SYROS during the [**] retention

term, QIAGEN shall provide to SYROS copies of all such Project Data at SYROS's expense.

4.4. Inspections, Audits, or Investigations of QIAGEN by Governmental Authorities. Upon reasonable and lawful request, QIAGEN will allow appropriate worldwide Governmental Authorities to inspect its facilities or review records relating to Activities.

(a) Non-Routine Matters. If any Governmental Authority gives QIAGEN notice of its intent, with respect to any QIAGEN facility that is performing a Project for SYROS under this Agreement, to conduct a non-routine inspection, audit, or investigation, or take any other type of regulatory action in relation to the Activities, QIAGEN will, unless prohibited by such Governmental Authority or Applicable Law, give SYROS written notice within [**] after QIAGEN's receipt of such notice thereof, if such inspection, audit or investigation is specific to a Project, and if notice cannot be provided to SYROS in advance of any such inspections, then QIAGEN will notify SYROS promptly and supply all relevant information and findings pertaining thereto.

(b) Cooperation. SYROS shall have the right to [**] during the course of any inspections, audits and investigations specifically related to the SYROS Product [**] impact the Regulatory Approval of the SYROS Product and/or the QIAGEN IVD, unless prohibited by Applicable Law or Governmental Authority, provided that [**]. QIAGEN will cooperate with the Governmental Authority (and keep SYROS representatives timely informed) in the conduct of such inspections, audits, and investigations and will maintain records of Activities in a way that facilitates the objectives of such activities.

(c) Inspection Findings and Responses. QIAGEN will provide regular updates to SYROS during the course of any audit performed pursuant to this Section 4.4. Within [**] of receipt, QIAGEN will forward to SYROS copies of any relevant reports and findings pertaining to the matters set forth in Section 4.4(a) to the extent related to the Activities or that would materially impact either QIAGEN's ability to obtain Regulatory Approval for, or ensure the clinical or commercial supply of, the Clinical Trial Assay or QIAGEN IVD being developed for SYROS under a Schedule. Whenever feasible and solely to the extent that it would not compromise the timeliness or quality of the response, QIAGEN will also provide SYROS with an opportunity to prospectively review and comment on any QIAGEN responses to Governmental Authorities that relate to Activities. Regardless of whether SYROS has an opportunity to prospectively

review and comment on any QIAGEN responses, QIAGEN will have the final say and determine the appropriate response and provide SYROS a copy of the response submitted to Governmental Authorities.

4.5. Audits of QIAGEN by SYROS. During the Term, SYROS shall have the right to audit or have audited QIAGEN's facility and records, and the facilities and records of QIAGEN's subcontractors, used for a Project, no more than [**]. QIAGEN agrees to maintain accurate and detailed records and information pertaining to any particular Project and agrees to grant access to SYROS (or its nominee, to be approved by QIAGEN, with such approval not to be unreasonably withheld) to perform such audit. Such audit(s) will require reasonable prior written notice, no less than [**] (other than an audit "for cause", in which case SYROS and QIAGEN shall cooperate reasonably to schedule the audit as expeditiously as possible while allowing QIAGEN reasonable time to prepare), by SYROS, and the auditor shall be subject to QIAGEN's reasonable confidentiality and site security policies. In addition, SYROS shall have the right to audit QIAGEN's facility and records related to a Project at any time "for cause." An "audit for cause" shall be defined as an audit of QIAGEN's facilities or records requested by SYROS and conducted by or on behalf of SYROS due to the existence of an operational issue in the manufacture of any component of the QIAGEN IVD that SYROS reasonably believes in good faith may result in a cGMP or other regulatory deficiency or failure of QIAGEN to meet its obligations under this Agreement (such as repeated failure of the QIAGEN IVD to meet its specifications, evidence of regulatory noncompliance and fraudulent data from any clinical trial conducted by or on behalf of QIAGEN), provided that SYROS notifies QIAGEN in writing in advance of such issue and the issue remains unresolved, to Syros' reasonable satisfaction, within a reasonable timeframe following QIAGEN's receipt of such written notice. Such audit(s) will require reasonable prior written notice by SYROS and shall be subject to QIAGEN's reasonable confidentiality and site security policies.

4.6. Financial Records. QIAGEN agrees to maintain for a period of [**] after the expiration or termination of this Agreement adequate and correct books and records relating to the performance of its material obligations hereunder and all costs and liabilities incurred hereunder, including records of, and copies of all receipts for third party expenses incurred in connection with the performance of the Activities and allow access to SYROS and its authorized representatives to inspect such records and receipts upon reasonable notice during ordinary business hours and subject to QIAGEN's reasonable and generally applicable confidentiality, site security and safety procedures.

4.7. Informed Consent. SYROS shall be responsible for obtaining any required informed consent documents signed by or on behalf of each human subject whose clinical sample will be provided by SYROS to QIAGEN as part of a Schedule. SYROS shall retain copies of such informed consents throughout the term of this Agreement and for a minimum period of [**] following the closure of the last clinical study of the SYROS Product or at least [**] after the last Regulatory Approval in a Market under this Agreement, whichever is later, and shall not destroy any records without prior written consent from QIAGEN. SYROS shall provide the template informed consent documents for each Clinical Trial relating to the Clinical Trial Assay to QIAGEN upon QIAGEN's reasonable request and will permit access to signed copies of such consents should evidence of signed consent be required in any audit or inspection by a Governmental Authority related to this Agreement. QIAGEN shall be responsible for obtaining any required informed consent documents signed by or on behalf of each human subject whose clinical sample may be acquired by QIAGEN as part of the Schedule. QIAGEN shall retain copies of such informed consents throughout the term of this Agreement and for a minimum period of [**] after the closure of the last clinical study of the QIAGEN IVD or at least [**] after the last Regulatory Approval in a Market under this Agreement, whichever is later, and shall not destroy any records without prior written consent from SYROS. QIAGEN shall provide copies of such consents to SYROS upon SYROS's reasonable request.

5. Interactions with Affiliates and Third Parties

5.1. Subcontractors.

(a) Either Party may involve any of its Affiliates in the performance of a Project without notice to or consent from the other Party. QIAGEN shall not engage or make use of any subcontractor or consultant (other than (i) individual consultants, (ii) distributors Commercializing the QIAGEN IVD in the Markets, and (iii) Clinical Affairs or Regulatory advisors) for the performance of the Activities (except as expressly set forth in the applicable Schedule) without SYROS' prior written consent, not to be unreasonably withheld, conditioned, or delayed. Each Party is and remains solely and exclusively responsible for the conduct of Activities by any Affiliate (and in the case of QIAGEN, any subcontractor or consultant), and any act or omission by an Affiliate (and in the case of QIAGEN, authorized subcontractor or consultant) that would constitute a breach of this Agreement by the applicable Party will be a breach of this Agreement by such Party.

(b) To the extent that a Party utilizes its Affiliates (or, in the case of QIAGEN, third party contractors) to perform tasks within the scope of a Project, such Party shall ensure all such third party contractors have entered into an appropriate written agreement with the Party obligating such person, and that all Affiliates are otherwise obligated to: (i) treat the other Party's Confidential Information in accordance with the provisions of Article 7, and (ii) assign rights to any Foreground Intellectual Property and/or Project Data so that such rights can be conveyed in accordance with the terms and conditions of Article 8, and (iii) with respect to QIAGEN, that its Affiliates or third party contractors grant audit and inspection rights similar to the right set forth in Sections 4.4 and 4.5; whereas the foregoing shall not limit QIAGEN's audit and inspection responsibilities. Each Party shall be liable and solely responsible for the acts, performance and compensation of its respective third party contractors.

5.2. Contract Laboratories. The Parties may use third party laboratories (hereinafter **"Contract Laboratories"**) for the performance of certain services, such as sample testing, in a Development Project pursuant to a Schedule. The terms for use of Contract Laboratories shall be set forth in a Schedule, but in the absence of provisions in a Schedule to the contrary, the following general principles shall apply:

(a) Contracts. SYROS shall be responsible for selecting and contracting with the Contract Laboratories engaged to assess the clinical validity of a Clinical Trial Assay or a QIAGEN IVD, subject to QIAGEN's prior consent which may only be withheld in case QIAGEN has reasonable quality concerns with respect to the performance of such sample testing by such Contract Laboratory.

(b) Certifications. SYROS and QIAGEN shall ensure that the Contract Laboratories are properly certified to perform the clinical validity work according to the applicable Schedule for the Project and this Agreement.

(c) Products and Equipment. QIAGEN shall be solely responsible for the manufacture and supply of a Clinical Trial Assay or a QIAGEN IVD, at SYROS' expense as set forth in the applicable Schedule, to the Contract Laboratories for clinical validity testing and for sufficient educating and training of the Contract Laboratories personnel as necessary for conducting the clinical validity testing. QIAGEN shall be responsible for ensuring that each such Contract Laboratory has or is provided the necessary equipment (including any upgrades) needed to perform any assay developed hereunder,

all of which shall be at SYROS' or the Contract Laboratory's expense, as agreed between SYROS and the Contract Laboratory .

6. Financial Terms

6.1. Milestones.

(a) Payments. QIAGEN shall be compensated for the performance of a Project on the basis of achievement of the milestones set forth in the Schedule.

(b) Acceptance Process. Upon completion of a milestone, QIAGEN shall issue a written notice to SYROS, together with any documentation reasonably requested by SYROS to evaluate such completion, and SYROS shall have up to [**] to review the notice and any associated Deliverables and provide a written acceptance of the milestone to QIAGEN. Failure to respond within this timeframe shall constitute acceptance. In the event SYROS disputes that a milestone has been properly completed, SYROS shall provide a written notice to QIAGEN within the initial [**] review period, describing in reasonable detail the basis for its dispute. The Parties shall work in good faith to resolve the dispute and QIAGEN shall use Commercially Reasonable Efforts to correct any deficiencies in a timely fashion. If the dispute is resolved by mutual agreement of the Parties that the particular milestone has been completed, then within [**] of the resolution of the dispute, SYROS shall issue a notice of written acceptance of the milestone to QIAGEN. If the dispute is resolved by mutual agreement of the Parties that the particular milestone has not been completed, then QIAGEN shall use Commercially Reasonable Efforts to complete any additional activities necessary to complete such milestone. If the Parties are unable to resolve such dispute, then it shall be resolved in accordance with Section 18.3.

(c) Invoicing. Upon receipt of SYROS's acceptance or upon expiration of the [**] review period as described above, QIAGEN shall issue an invoice to SYROS for the relevant Milestone Payment and send such invoice to the following address: [**]

6.2. Pass-through Costs and Expenses.

(a) Reimbursement. SYROS shall reimburse QIAGEN for the direct, out-of-pocket expenses incurred by QIAGEN in the performance of a Project without mark-up or surcharge ("Pass-through Costs and Expenses") and agreed by

the Parties in advance according to the Schedule. QIAGEN shall invoice SYROS for such expenses on a quarterly basis.

(b) Currency Conversion. Any Pass-through Costs and Expenses that were incurred in a currency other than USD shall be converted into USD using the average of the fixing exchange rates published by Bloomberg under the function "BFIX" for the respective currency at noon New York time for the applicable calendar quarter. If, on any Business Day, no USD foreign exchange fixing rate is determined by Bloomberg for the relevant currency, the last Bloomberg price of such day (data field "PX last") shall be used instead.

6.3. Undisputed Amounts. SYROS shall pay all undisputed amounts set forth in any invoice in US Dollars ("USD") within [**] of receipt from QIAGEN.

6.4. Payment Disputes. In the event SYROS disputes an invoice from QIAGEN in good faith, SYROS shall notify QIAGEN of its dispute within the [**] payment terms and provide sufficient detail for QIAGEN to investigate the issue. SYROS shall pay any portion of the invoice not in dispute within the original [**] payment terms. The Parties shall work together in good faith to resolve payment disputes in a timely fashion.

6.5. Late Payments.

(a) Interest. In the event SYROS fails to pay an invoice according to the payment terms, and has not notified QIAGEN of a good faith dispute with such invoice, QIAGEN shall have the right to charge interest, commencing on the due date (inclusive) and ending on the actual payment date (exclusive), calculated at a rate of [**]% per month or the maximum amount permitted under Applicable Law, whichever is lower.

(b) Suspended Performance. If SYROS fails to make an undisputed payment under a Schedule within [**] after the date when due, then QIAGEN shall be entitled, in addition to any other remedies hereunder, to provide SYROS with [**] notice of its intention to suspend its performance under such Schedule until the due amount has been paid.

6.6. Taxes.

(a) All agreed remunerations/fees are considered to be net of value added tax (hereinafter "VAT"). VAT will be due additionally as legally owed to the

applicable jurisdiction, payable after receipt of a proper invoice, which meets all legal requirements according to the applicable VAT-law.

(b) To the extent that the goods or services to be provided hereunder are subject to any sales, use, rental, personal property, or any other transaction or indirect taxes under law, payment of said taxes is SYROS's responsibility, subject to any applicable exemption entitlement.

(c) Any Party required to make a payment (hereinafter the "Paying Party") to the other Party (hereinafter the "Payee") under this Agreement shall be entitled to deduct and withhold from the amount payable the withholding tax for which the Paying Party is liable under any provisions of tax law. Any withheld tax shall be treated as having been paid by Paying Party to Payee for all purposes of this Agreement. Paying Party shall timely forward the tax receipts certifying the payments of withholding tax on behalf of Payee. In case Paying Party cannot deduct the withholding tax due to fulfilment completion of payment obligation by settlement or set-off, Payee will pay the withholding tax to Paying Party separately. If Paying Party failed to deduct withholding tax but is still required by tax law to pay withholding tax on account of Payee to the tax authorities, Payee shall assist Paying Party with regard to all procedures required in order to obtain reimbursement by tax authorities or, in case tax authorities will not reimburse withholding tax to Paying Party, Payee will immediately refund the tax amount.

7. Confidentiality

7.1. Use of Confidential Information. In connection with this Agreement and individual Projects, the Parties anticipate that each Party will disclose Confidential Information to the other Party in order to facilitate the performance of their respective obligations thereunder (the "Purpose"). Therefore, each Party shall: (i) only use Confidential Information of the other Party for the Purpose, (ii) maintain the disclosing Party's Confidential Information in confidence using the same degree of care that it uses for its own Confidential Information of like importance, but in no event using less than reasonable care, and (iii) not disclose or transfer any Confidential Information of the disclosing Party (or any materials which contain such Confidential Information), to any third party without the disclosing Party's consent; provided, however, that disclosure shall be permitted to the receiving Party's employees, directors, officers, advisors (including accountants, attorneys, consultants and financial advisors), or permitted subcontractors (and those of its Affiliates) who reasonably require

such Confidential Information for the Purpose and who are bound by obligations of non-use and confidentiality with respect to such Confidential Information no less restrictive than those set forth in this Article 7. Notwithstanding the foregoing, SYROS, as the Receiving Party, may disclose Confidential Information to (A) [**] of the SYROS Product, or potential or actual investors or acquirers of SYROS or that portion of SYROS' business relating to the SYROS Product; *provided* that such [**], investors, or acquirers shall be subject to commercially reasonable obligations of confidentiality and non-use with respect to such Confidential Information; and *provided*, *further*, that if a [**], investor, or acquirer has a [**], SYROS shall seek QIAGEN's written consent prior to making the disclosure, such consent not to be [**], and if QIAGEN consents, SYROS shall take reasonable steps (including[**], if necessary) to ensure that such Confidential Information is not disclosed to employees or agents engaged in the [**], and SYROS shall remain liable to QIAGEN for any breach by such third parties of the confidentiality obligations owed to QIAGEN; (B) Governmental Authorities as reasonably required for any filing, application or request for Regulatory Approval of the SYROS Product; or (C) any patent authority as reasonably required for seeking or maintaining patent rights with respect to any SYROS Product, Without limitation to the foregoing, SYROS, as the Receiving Party, may also disclose the terms of this Agreement to (A) potential or actual investors or acquirers of SYROS or that portion of SYROS' business relating to the SYROS Product, and (B) SYROS' attorneys or investment bankers; *provided* that such persons shall be subject to written, or in the case of attorneys, fiduciary or professional, obligations of confidentiality and non-use with respect to such Confidential Information no less restrictive than those set forth in this Agreement and SYROS shall remain liable to QIAGEN for any breach by such third parties of the confidentiality and non-use obligations owed to QIAGEN.

Non-Confidential Information. The obligations set forth in Section 7.1 shall not apply to any information that the receiving Party can demonstrate by competent proof: (i) was possessed or already known by the receiving Party or any of its Affiliates prior to disclosure under this Agreement, (ii) was developed by the receiving Party or any of its Affiliates independently from disclosure or development under this Agreement and without reference to or reliance upon Confidential Information of the disclosing Party, (iii) is now or becomes later publicly available other than by breach of this Agreement by receiving Party or any of its Affiliates, or (iv) is available to the receiving Party or any of its Affiliates from a third party that is not legally prohibited from disclosing such information.

7.2. Compelled Disclosure. In the event a receiving Party is compelled by legislative, governmental or judicial order to disclose the Confidential Information of the disclosing Party, the receiving Party shall take reasonable steps to give the disclosing Party sufficient prior notice in order to allow the disclosing Party an opportunity to contest such order or seek a protective order at the expense of the disclosing Party. In the event the receiving Party is ultimately required to disclose such Confidential Information, the receiving Party shall disclose only such portion of the Confidential Information that is legally required to be disclosed and shall seek, at the disclosing Party's request and expense, a protective order to protect the confidentiality of such Confidential Information.

7.3. SEC Filings. The Receiving Party may disclose the terms of this Agreement if, in the opinion of the Receiving Party's counsel, such disclosure is required by Applicable Law or the rules of a stock exchange on which the securities of the Receiving Party are listed (or to which an application for listing has been submitted); *provided* that the Receiving Party shall (A) submit the proposed disclosure in writing to the Disclosing Party as far in advance as reasonably practicable (and in no event less than [**] prior to the anticipated date of disclosure) so as to provide a reasonable opportunity to comment thereon; (B) make itself available for discussion of such proposed disclosure; and (C) consider in good faith the comments of the Disclosing Party with respect to such proposed disclosure. The Receiving Party shall consider in good faith the Disclosing Party's reasonable requests to modify or redact the disclosure to protect the Disclosing Party's Confidential Information. The Receiving Party shall also, as promptly as practicable, provide the Disclosing Party with a copy of the relevant portions of any SEC comment letter or other communication that expresses an objection by the SEC staff to any redaction or omission of information about, or specific terms or provisions of, the Agreement or any Schedule from such filing, and before publicly disclosing such information or restoring the redacted terms or provisions in the filing, give the Disclosing Party the opportunity to participate in drafting a response to such comments and incorporate the Disclosing Party's reasonable requests to include in such response the rationale for omitting or redacting such information, terms or provisions. The Receiving Party shall use reasonable efforts to maintain confidential treatment of any disclosure made pursuant to this Section 7.3, including by filing applications for extension with the SEC of any confidential treatment order, during the Term of this Agreement and for a period of [**] thereafter.

7.4. Initial Press Release. Upon execution of this Agreement, each Party shall have the right to issue an initial press release announcing the execution of this Agreement, provided that the Party wishing to make the disclosure shall: (a) provide the other Party a draft of such announcement at least [**] prior to its public release; and (b) reasonably consider any comments provided by the other Party with respect to such announcement. Following such initial press release, neither Party may make (or have made on its behalf) any oral or written release of any statement, information, advertisement or publicity in connection with this Agreement or any Schedule unless such statement includes only those facts that were initially released in accordance with the first sentence of this Section 7.4. In addition, neither Party shall use the other Party's name, symbols, or trademarks in any statement, information, advertisement or publicity without the other Party's prior written approval.

7.5. Equitable Relief. Each Party agrees that damages may not be an adequate remedy for breach of this Article 7 and that, accordingly, either Party shall be entitled to seek injunctive or other equitable relief to prevent disclosure of its Confidential Information.

8. Data

8.1. Assignment and License Back of Project Data. All Project Data shall be owned as follows:

(a) SYROS shall own all Clinical Data. SYROS shall be free to use the Clinical Data for any purpose. QIAGEN shall disclose and provide to SYROS any and all Clinical Data generated by QIAGEN or its Affiliates and Representatives. QIAGEN, as far as it is in the legal position to do so, hereby assigns all of its right, title and interest in and to such Clinical Data to SYROS.

(b) SYROS shall own all SYROS Biomarker Data. SYROS shall be free to use the SYROS Biomarker Data for any purpose. QIAGEN shall disclose and provide to SYROS any and all SYROS Biomarker Data generated by QIAGEN or its Affiliates or Representatives. QIAGEN, as far as it is in the legal position to do so, hereby assigns all of its right, title and interest in and to such SYROS Biomarker Data to SYROS.

(c) QIAGEN shall own all QIAGEN Biomarker Data. QIAGEN shall be free to use the QIAGEN Biomarker Data for any purpose. SYROS shall disclose and provide to QIAGEN any and all QIAGEN Biomarker Data generated by SYROS or its Affiliates or Representatives. SYROS, as far as it is in the legal

position to do so, hereby assigns all of its right, title and interest in and to such QIAGEN Biomarker Data to QIAGEN.

(d) QIAGEN shall own all Analytical Performance Data. QIAGEN shall be free to use the Analytical Performance Data for any purpose. SYROS shall disclose and provide to QIAGEN all Analytical Performance Data generated by SYROS or its Affiliates or Representatives. SYROS, as far as it is in the legal position to do so, hereby assigns all of its right, title and interest in and to such Analytical Performance Data to QIAGEN.

(e) SYROS hereby grants to QIAGEN a non-exclusive, world-wide, royalty-free license and right of reference to the Clinical Data and the SYROS Biomarker Data, with the right to sublicense to QIAGEN's Affiliates or any third party developing, obtaining Regulatory Approval for, manufacturing or selling the QIAGEN IVD under the Project on behalf of QIAGEN, for the sole and limited purpose of, and only to the extent required to carry out its Activities under the Project, including subsequent Commercialization of the QIAGEN IVD developed within the Project for use with the SYROS Product. QIAGEN shall not use the Clinical Data or SYROS Biomarker Data for any purpose other than permitted in this Section 8.1(e) for as long as such Clinical Data or SYROS Biomarker Data constitutes Confidential Information.

(f) QIAGEN hereby grants SYROS a non-exclusive license and right of reference to the Analytical Performance Data and QIAGEN Biomarker Data for the sole and limited purpose of, and only to the extent required to, carry out the Activities under the Project and research, develop and/or obtain Regulatory Approval for, make, have made, use, sell, offer for sale, import, export and commercialize SYROS Products with the QIAGEN IVD. The license shall not be sub-licensable other than to one of SYROS' Affiliates or to a third party researching, developing, obtaining Regulatory Approval for, making, having made, using, selling, offering for sale, importing, exporting or Commercializing the SYROS Product with the QIAGEN IVD, whether alone or in collaboration with SYROS or any of its Affiliates. All sub-licenses by SYROS shall be "first-tier," meaning the sublicensee shall have no further right to sublicense. SYROS shall not use the Analytical Performance Data or QIAGEN Biomarker Data for any purpose other than permitted in this Section 8.1(f) for as long as such the Analytical Performance Data or QIAGEN Biomarker Data constitutes Confidential Information.

9. Intellectual Property

9.1. Background Intellectual Property. Each Party acknowledges and agrees that the other Party Controls certain Background Intellectual Property that relates to that Party's business or operations. Each Party further acknowledges and agrees that Background Intellectual Property Controlled by the other Party shall, as between the Parties, remain the exclusive property of the other Party.

Each Party hereby grants to the other Party a non-exclusive, world-wide, non-sub-licensable, non-transferable and royalty-free license under its Project-Related Background Intellectual Property to the extent such license is necessary for the other Party to carry out its Activities under the respective Project, including subsequent Commercialization by QIAGEN of the QIAGEN IVD developed in the respective Project for use with the respective SYROS Product and subsequent Commercialization by SYROS of the SYROS Product with the QIAGEN IVD under this Agreement. For the avoidance of doubt, the Parties agree that the foregoing license does not provide QIAGEN any right to promote or Commercialize a SYROS Product or any other drug. For the further avoidance of doubt, the Parties agree that the foregoing license does not provide SYROS any right to promote or Commercialize the QIAGEN IVD or any other IVD or laboratory developed test.

Notwithstanding the foregoing, if Intellectual Property controlled by a third party is included in the Background Intellectual Property of a Party, such Intellectual Property shall only be included into the license grant of this Section 9.1 paragraph 2, if (i) the other Party has committed in writing to comply with the relevant terms and conditions of the agreement with the third party and (ii) if applicable, the Parties have agreed in writing on the allocation or sharing of any payment obligations towards the third party which may result from the other Party's use of the third party's Intellectual Property. In addition, if the relevant (license) agreement with such third party requires an allocation of Project Data and Foreground Intellectual Property or licenses deviating from Sections 8 and 9.2, (i) the Controlling Party shall inform the other Party hereof and (ii) upon request of the other Party to include such third party's Intellectual Property into the license grant under this Section 9.1, the Parties shall negotiate in good faith provisions deviating from Sections 8 and 9.2 and set them forth in writing. For the avoidance of doubt, the foregoing shall also apply to third party Intellectual Property acquired pursuant to Section 9.6.

9.2. Foreground Intellectual Property. The Parties agree that any Foreground Intellectual Property shall be treated as follows:

(a) SYROS Foreground IP. SYROS shall exclusively own all right, title and interest in and to any SYROS Foreground IP. SYROS hereby grants to QIAGEN a non-exclusive, world-wide, royalty-free license, with the right to sublicense, under the SYROS Foreground IP for carrying out the Activities under the respective Project, including subsequent Commercialization of a QIAGEN IVD developed within a Project for use with the respective SYROS Product.

(b) QIAGEN Foreground IP. QIAGEN shall exclusively own all right, title and interest in and to any QIAGEN Foreground IP. QIAGEN hereby grants to SYROS a non-exclusive, world-wide license, with the right to sublicense, under the QIAGEN Foreground Intellectual Property for carrying out the Activities under the respective Project, including subsequent Commercialization of the SYROS Product with (i) the QIAGEN IVD in the Markets, in which case the license shall be royalty-free, or (ii) [**].

(c) Joint Foreground IP. The Parties shall jointly own an equal, undivided interest in and to any Joint Foreground IP. In the event that a jurisdiction requires consent of co-owners for one co-owner to grant license rights under or otherwise exploit Joint Foreground IP, each Party hereby grants to the other Party and its Affiliates a sublicensable right and license to exploit such Joint Foreground IP without a requirement of accounting other than as set forth in this Agreement.

(d) Protection of Either Party's Foreground Intellectual Property. The Parties will inform each other about any Foreground Intellectual Property without unreasonable delay after it has been conceived by their Representatives. The Parties shall take all legally required steps to ensure and effect the allocation of the Foreground Intellectual Property as provided in Sections 9.2(a)-(c) at the sole expense of the Party owning the Foreground Intellectual Property according to Sections 9.2(a)-(c) and, the other Party shall provide reasonable assistance and all necessary documentation and declarations to perfect the rights in the Foreground Intellectual Property (e.g., documents for proof of chain of title). Each Party will provide the other Party with [**] prior notice before pursuing patent protection on the Foreground Intellectual Property allocated to it according to Sections 9.2(a)-(c). QIAGEN shall be responsible, at its own expense, for the preparation, filing, prosecution and maintenance of QIAGEN Foreground IP and SYROS shall be responsible, at its own expense, for the preparation, filing, prosecution and maintenance of the SYROS Foreground IP. The Parties shall discuss in good faith allocations of

responsibility for the preparation, filing, prosecution and maintenance of the Joint Foreground IP.

9.3. Defense and Enforcement. Each Party shall promptly notify the other Party in the event it becomes aware of any third party activities that may constitute infringement of any Intellectual Property that is the subject to this Agreement and/or of any third party claims or allegations contesting the validity and/or enforceability of any such Intellectual Property. QIAGEN shall have the right, but not the obligation, to control, enforce and defend worldwide, at its own expense, Intellectual Property rights in the QIAGEN Background Intellectual Property and QIAGEN Foreground IP. SYROS shall have the right, but not the obligation, to control, enforce and defend worldwide, at its own expense, Intellectual Property rights in the SYROS Background Intellectual Property and SYROS Foreground IP. With respect to any Joint Foreground IP, the Parties will promptly thereafter consult and cooperate to determine a course of action.

9.4. Trademarks

(a) The Parties shall be responsible for the selection, registration and maintenance of the Trademarks they employ in connection with the marketing, sale or distribution of their respective Products (i.e., the SYROS Product in the case of SYROS and the QIAGEN IVD in the case of QIAGEN). The Parties shall own and control their respective Trademarks and pay all relevant costs thereto.

(b) SYROS shall have the sole right to select the SYROS Trademarks and shall own and retain all right, title and interest in and to such SYROS Trademarks, and all goodwill associated with or attached to the SYROS Trademarks arising out of the use thereof by SYROS, its Affiliates and third party licensees shall inure to the benefit of SYROS. Only SYROS will be authorized to initiate at its own discretion legal proceedings against any infringement or threatened infringement of the SYROS Trademarks.

(c) SYROS shall be responsible for the registration, hosting, maintenance and defence of the SYROS Domain Names. For the avoidance of doubts, SYROS is allowed to register such Domain Names in its own name, to host on its servers, maintain and defend these Domain Names and use them for websites.

(d) QIAGEN shall have the sole right to select the QIAGEN Trademarks and shall own and retain all right, title and interest in and to such QIAGEN Trademarks,

and all goodwill associated with or attached to the QIAGEN Trademarks arising out of the use thereof by QIAGEN, its Affiliates and third party licensees shall inure to the benefit of QIAGEN. Only QIAGEN will be authorized to initiate at its own discretion legal proceedings against any infringement or threatened infringement of the QIAGEN Trademarks.

(e) QIAGEN shall be responsible for the registration, hosting, maintenance and defence of the QIAGEN Domain Names. For the avoidance of doubts, QIAGEN is allowed to register such Domain Names in its own name, to host on its servers, maintain and defend these Domain Names and use them for websites.

(f) The Parties recognize the exclusive ownership of each other Party's Trademarks, logotype or trade dress furnished by such Party for use in connection with the marketing, sale or distribution of the Product as defined in this Agreement. The Parties shall not, either while this Agreement is in effect, or at any time thereafter, register, use or challenge or assist others to challenge each other Party's Trademarks, logotype and trade dress furnished by each Party for use in connection with the marketing of the products as defined in this Agreement or attempt to obtain any right in or to any such name, logotype, trademarks or trade dress confusingly similar for the marketing of the products as defined in this Agreement or any other goods and products, notwithstanding that such goods or products have a different use or are dissimilar to the products as defined in this Agreement.

(g) Each Party hereby grants to the other Party a non-exclusive, world-wide, sub-licensable, non-transferable and royalty-free license under its Trademarks relevant for a Project to the extent such license is necessary for the other Party to carry out its Activities under the respective Project, including subsequent Commercialization by QIAGEN in accordance with Section 11 of this Agreement of the QIAGEN IVD developed in the respective Project for use with the respective SYROS Product and subsequent Commercialization by SYROS of the SYROS Product with the QIAGEN IVD under this Agreement.

9.5. Notice of a Third Party's Claim of Intellectual Property Infringement During a Project, the Parties will promptly notify each other of any claim by a third party that the Development or Commercialization of the SYROS Product or QIAGEN IVD may or does infringe any Intellectual Property right Controlled by a third party.

9.6. Third Party Intellectual Property Licenses

(a) Licenses relevant for the SYROS Product. SYROS shall be solely responsible, at its own discretion and expense, for obtaining and maintaining any licenses or other rights to access or use any third party Intellectual Property that is necessary for the development, manufacture, use or Commercialization of any SYROS Product, including but not limited to treatment decisions derived from a diagnostic result and/or patient selection and/or stratification and/or biomarkers. QIAGEN agrees to cooperate reasonably with SYROS to assist SYROS's acquisition of any licenses that it is obligated to obtain pursuant to Section 9.6(a) or 9.6(c); [**].

(b) Licenses Relevant for the QIAGEN IVD System. QIAGEN shall be solely responsible, at its own discretion and expense, for obtaining and maintaining any licenses or other rights to access or use any third party Intellectual Property that is necessary for the development, manufacture, use or Commercialization of the QIAGEN IVD System or the use of the QIAGEN IVD for [**] pursuant to this Agreement.

(c) Licenses Relevant to Biomarkers. The intellectual property landscape for the diagnostic use of any Biomarkers used in connection with the development, manufacture, use or Commercialization of the QIAGEN IVD ("Third Party Biomarker IP") shall be assessed on a project-by-project basis. The Parties shall mutually agree upon, and explicitly set forth in each Project Schedule, which Party will bear the responsibility (or whether responsibility will be shared) for conducting a freedom-to-operate ("FTO") inquiry to assess the need to obtain any licenses or other rights to access or use any Third-Party Biomarker IP. The Party responsible for such inquiry shall [**]. Based on the results of the FTO inquiry, the Parties shall [**]. In the event that (a) [**], or (b) [**], then either Party may terminate the applicable Project Schedule pursuant to Section 13.1(d). For clarification, (i) except as set forth in a Project Schedule, [**], and (ii) [**], shall not be considered a breach of this Agreement.

9.7. No Other Rights. Except as expressly provided herein, nothing in this Agreement shall be construed as a grant from one Party to the other Party of any rights in or title to any Intellectual Property, Material, or Confidential Information.

10. Regulatory Matters. SYROS shall be responsible for obtaining Regulatory Approval for the SYROS Product. QIAGEN shall use Commercially Reasonable Efforts to support any efforts of SYROS to obtain Regulatory Approval for the SYROS Product for use

with the QIAGEN IVD in each Market. QIAGEN shall be responsible for obtaining and maintaining Regulatory Approvals for the QIAGEN IVD in each Market agreed by the Parties in a Schedule. For clarification, any post-Regulatory Approval requirements imposed by a Governmental Authority that were not anticipated in the Schedule shall be discussed between the Parties in good faith, and QIAGEN shall have no obligation to undertake such requirements until they have been included in the relevant Schedule by a written amendment thereto. QIAGEN shall be the sponsor of, and bear all responsibility to make Regulatory Submissions for the QIAGEN IVD, with reasonable cooperation and support from SYROS as appropriate. QIAGEN shall remain solely responsible for all interactions with Governmental Authorities with respect to the QIAGEN IVD but with respect to such Regulatory Submissions shall (a) reasonably consult with SYROS as to the portions of the submission that refer to the SYROS Product , (b) consider in good faith SYROS' reasonable comments on such submissions that refer to the SYROS Product and (c) shall keep SYROS reasonably informed regarding the status and progress of all regulatory activities regarding obtaining Regulatory Approval of the QIAGEN IVD, including as promptly as reasonably practicable. In addition, QIAGEN shall provide SYROS with a copy of all final Regulatory Submissions (or applicable portions thereof), filings or other material documentation provided from or to any Governmental Authority as contemplated by this Agreement that refer to the SYROS Product, after submission to the relevant Governmental Authority, and promptly inform SYROS regarding the receipt or denial of Regulatory Approval for the use of the QIAGEN IVD in connection with theSYROS Product. In addition, QIAGEN will, at SYROS's request, permit SYROS to participate with QIAGEN in preparations for any substantive correspondence, communications or meetings with Governmental Authorities which involve substantive discussion of the SYROS Product and [**] such substantive correspondence, communications or meetings with Governmental Authorities, in each case, where the anticipated focus of such correspondence, communication or meeting is related to the use of the QIAGEN IVD in connection with a SYROS Product, to the extent permitted by any Applicable Law.

11. Clinical Trials.

11.1. QIAGEN Responsibilities. QIAGEN will develop the Clinical Trial Assay or QIAGEN IVD for use as a companion diagnostic for the SYROS Product and shall be responsible for (a) providing oversight over any testing of patient samples from the corresponding Clinical Trial with the Clinical Trial Assay or QIAGEN IVD and (b) any other Activities related to the corresponding Clinical Trial with the Clinical Trial Assay or QIAGEN IVD, in each case, as described in the applicable Schedule. QIAGEN shall conduct all such Activities for which it is

responsible pursuant to this Section 11.1 in compliance with Applicable Law, including but not limited to 21 C.F.R. § 812 (and its foreign equivalents) and in accordance with the applicable Schedule. QIAGEN will bear responsibility for meeting all applicable regulatory requirements for the development and manufacture of the Clinical Trial Assay or QIAGEN IVD in each Market in which the Clinical Trial Assay or QIAGEN IVD is used as part of a Clinical Trial. QIAGEN will promptly provide to SYROS notice and a description of material progress and developments under all such Clinical Trials.

11.2. SYROS Responsibilities. SYROS will have sole responsibility for the control and direction of the conduct of all Clinical Trials for each SYROS Product, including through the use of contract research organizations, in its sole discretion. Other than those Clinical Trials that are to be performed in whole or in part by QIAGEN pursuant to a Schedule, the conduct of all Clinical Trials by SYROS will not be governed by or included within the scope of this Agreement.

12. Manufacture and Supply of Clinical Trial Assays and IVDs.

QIAGEN shall use Commercially Reasonable (it being understood for the purpose of this Section 12 that [**] shall be taken into account when considering [**]) Efforts to, manufacture Clinical Trial Assays and QIAGEN IVDs, as applicable. QIAGEN shall manufacture the Clinical Trial Assays and QIAGEN IVDs in compliance with Applicable Law, the specifications and requirements set forth in the applicable Schedule, including, if applicable, cGMP requirements. Until Commercialization of a QIAGEN IVD, QIAGEN shall use Commercially Reasonable Efforts to ensure that adequate supplies of the Clinical Trial Assay and all other components of the QIAGEN IVD System are each made available to SYROS, any Contract Laboratories and any Clinical Trial sites, in each case according to the terms set forth in Section 5.2(c) and the relevant Schedule. Subject to receiving sufficient notice of required quantities from SYROS as required in the relevant Schedule, QIAGEN shall use Commercially Reasonable Efforts to maintain sufficient inventories of each component of the QIAGEN IVD System as is necessary for the complete conduct of the Clinical Trials of the applicable SYROS Product. QIAGEN shall be responsible for the transfer of the Clinical Trial Assay or the QIAGEN IVD thereof and all other components of the QIAGEN IVD System, to the Contract Laboratories and to the extent necessary, any Clinical Trial Sites involved in the Clinical Trials.

13. Commercialization of the QIAGEN IVD

13.1. Sales and Marketing Activities. QIAGEN shall be responsible to use Commercially Reasonable Efforts to Commercialize or have Commercialized the QIAGEN IVD in each Market. QIAGEN shall use Commercially Reasonable

Efforts to perform the Commercialization Activities under each Schedule. Once the SYROS Product receives Regulatory Approval in a given Market, and once the QIAGEN IVD receives Regulatory Approval, QIAGEN agrees to use Commercially Reasonable Efforts to make the QIAGEN IVD commercially available in that Market. Provisions related to security of supply, safety stock and other matters designed to ensure QIAGEN's ability to ensure sufficient inventories of the Clinical Trial Assay and the QIAGEN IVD will be set forth as agreed to by the Parties in a Schedule for such Activities.

13.2. Diagnostics Reimbursement. In the event the Parties agree to conduct Activities relating to health insurance reimbursement for the QIAGEN IVD, such Activities shall be outlined in a Schedule.

13.3. Medical Affairs Activities. In the event the Parties agree to conduct Activities relating to medical affairs activities for the QIAGEN IVD, such Activities shall be outlined in a Schedule.

13.4. Continued Supply. Without limitation to any other remedies available to SYROS under this Agreement or otherwise, if, for any reason (other than to the extent due to the fault of SYROS or its Affiliates, including, but not limited to, insufficient notice of required quantities) QIAGEN is unable to supply the QIAGEN IVD in numbers sufficient to meet the requested demand therefore for a period of [**], then, until [**] following the date that QIAGEN is in a position again to fulfil such demand (the "Supply Resumption Date"), [**] after the Supply Resumption Date. Additionally, [**]. The foregoing [**], provided that SYROS may [**]. Any additional [**] shall be subject to [**]. All [**] shall be [**]. In addition, the [**], SYROS shall be [**].

14. Governance

14.1. Joint Steering Committee. Within [**] after the Effective Date, the Parties shall form a Joint Steering Committee (the "**JSC**") to facilitate the transfer of information and coordinate processes related to the development, Regulatory Approval and Commercialization of the SYROS Products and the QIAGEN IVDs being the subject of this Agreement. The JSC shall be composed of [**] representatives appointed by each Party, at least [**] of which shall be different than members of the JPT. Each representative shall be appointed (and may be replaced at any time) by a Party upon prior written notice to the other Party. These representatives shall have appropriate experience, knowledge, and ongoing familiarity with the Projects in their then current phases.

14.2. Responsibilities. The JSC's responsibilities shall include, but not be limited to, the following functions:

(a) reviewing the progress of the development Activities and ensuring that the development Activities commence and proceed according to each Schedule;

(b) approval of the scope and content of additional Schedules, and discussing and approving decision points set forth in each Schedule (provided that each such Schedule remains subject to final approval of and execution by authorized representatives of the respective Parties);

(c) discussing proposed amendments, modifications or changes to a Schedule which may be escalated by the JPT, including the scope of the Development Activities and budget, Deliverables and timelines and submitting such amendments for approval and execution by the respective Parties;

(d) facilitating the cooperation of the Parties, when requested, to provide information and support;

(e) approving each Schedule prepared by the JCC and submitting such Schedule for final approval of and execution by authorized representatives of the respective Parties;

(f) taking such other actions as may be specifically allocated to the JSC by the Parties, or escalated to the JSC by the JPT pursuant to Section 14.7, from time to time;

(g) resolving issues or disagreements raised by the JPT, JCC or Functional Leaders (as defined below);

(h) such other activities pertaining to the development and Commercialization Activities ascribed to the JSC in this Agreement or as mutually agreed between the Parties from time to time (including the formation or disbandment of any subcommittees).

14.3. Meetings. The JSC shall meet (either in person, telephonically or via video conference) at the frequency as agreed by the respective committee members, but no less than [**] times per year. Meetings of the JSC shall be at such locations as the Parties agree. The JSC shall be led by two (2) co-chairs, one (1) appointed by QIAGEN and one (1) appointed by SYROS. The JSC shall make decisions by consensus, with QIAGEN and SYROS each having one vote.

In the event of an impasse, the matter shall be resolved pursuant to Section 14.5. The responsibility for organizing the meeting, drafting the meeting agenda and drafting and finalizing the meeting minutes shall alternate between SYROS and QIAGEN. Additionally, upon invitation by the JSC or one or the other Party, JPT or JCC members or other Functional Leaders (as defined below) may attend JSC meetings as non-voting members and each JSC member may reasonably invite other guests to the meetings, in order to discuss special technical, regulatory, financial, or commercial topics relevant to the applicable agenda; provided that all guests are subject to the confidentiality provisions set forth in Article 7, in each case subject to the other Party's prior consent which shall not be unreasonably withheld, conditioned or delayed.

14.4. JSC Minutes. The JSC shall keep accurate and complete confidential minutes of its meetings. SYROS and QIAGEN will take turns in drafting the minutes of the JSC meetings. The chair of the Party responsible for drafting the minutes for such JSC meeting, or its respective designee, shall be responsible for taking such minutes and distributing them to the other JSC members for their review and comment within [**] after the date of each meeting, and within [**] after the receipt thereof, the other JSC members shall remit such minutes back to the chair with their comments, if any. The JSC members shall in good faith attempt as quickly as is reasonably possible to resolve any disputes as to the content of such minutes so as to have a final agreed version as quickly as is reasonably possible. Each of QIAGEN and SYROS shall be responsible for all expenses incurred by its representatives on the JSC in connection with performing its duties hereunder, including all costs of travel, lodging and meals.

14.5. JSC Decisions. All decisions of the JSC shall be made in good faith in the interest of furthering the purposes of this Agreement and the JSC members shall use good faith efforts to make decisions by consensus. If the JSC is unable to agree on any matter after good faith attempts to resolve such disagreement in a reasonable fashion, either of the co-chairs of the JSC may refer the disagreement to a meeting (either in person, telephonically or via video conference) between the senior executives of each Party (each Party shall promptly designate a senior executive with requisite authority to resolve the dispute, hereinafter referred to individually as a "Senior Executive" and collectively as the "Senior Executives") which meeting shall take place as soon as practicable, but in no event later than [**] after the date of the relevant referral. If the Senior Executives cannot resolve such disagreement over such matter in a mutually acceptable manner within [**] after such meeting then the matter shall be decided in accordance with Section 18.3. Notwithstanding the

foregoing, except as otherwise provided in this Agreement: (a) SYROS shall have the unilateral right to make final decisions that solely impact the development, manufacture, Regulatory Approval or Commercialization of the SYROS Product; provided that SYROS shall not be entitled to make a unilateral decision which imposes a financial obligation on QIAGEN or which deviates from the previously approved Schedule or which is inconsistent with or in excess of QIAGEN's obligations under this Agreement, and (b) QIAGEN shall have the unilateral right to make final decisions that solely impact the development, manufacture, Regulatory Approval or Commercialization of the QIAGEN IVD, provided that QIAGEN shall not be entitled to make a unilateral decision which imposes a financial obligation on SYROS or which deviates from the previously approved Schedule or which is inconsistent with or in excess of SYROS's obligations under this Agreement. Notwithstanding the foregoing, QIAGEN shall have the unilateral right to make final decisions on matters relating to the safety or performance of the QIAGEN IVD. For the avoidance of doubt, the JSC shall not have the authority to make decisions that are contrary to the terms and conditions of this Agreement, to amend this Agreement, or to amend any Schedule.

14.6. Joint Project Team.

Within [**] of the Effective Date of a Schedule, the Parties will, in addition to the JSC, form a joint project team for the applicable Project (the "**Joint Project Team**" or "**JPT**"), which shall be responsible for coordinating all operational tasks required for the development, regulatory, and other business and technical activities under the Project and providing updates on the status of the Project. The JPT shall be comprised of [**] Project team members in total ([**] members from QIAGEN and [**] members from SYROS. Each Party will designate a representative as its JPT lead (the "JPT Lead") who shall be the principal technical point of contact for that Party, and who shall be responsible for implementing and coordinating all technical activities, and facilitating the exchange of technical information between the Parties under this Agreement. Members of the JPT can include but shall not be limited to representatives with expertise in research biology, translational medicine, clinical, regulatory, product development and/or commercialization. As the Activities under the Schedule progress, the Parties anticipate that each Party shall designate an assay development leader, a regulatory leader, and, depending on the stage of the Schedule, a clinical leader or a commercial leader (collectively, the "Functional Leaders") who shall be the principal points of contact for each Party for matters relating to its respective function, and shall be responsible for implementing and

coordinating all activities and facilitating the exchange of information between the Parties for his or her function. Such JPT shall meet, either in person, via telephone or video conferences, on a regular basis, however, at least [**]. For the avoidance of doubt, the JPT shall not have the authority to make decisions that are contrary to the terms and conditions of this Agreement, to amend this Agreement, or to amend any Schedule. The members of the JPT shall cooperate with each other and work in good faith to resolve any disagreements between them or their respective teams. Any such disagreements that are not resolved by the JPT shall be escalated to the JSC for resolution. The JPT shall keep accurate and complete records of its activities and meetings and shall, from time to time as requested by the JSC, provide the JSC with appropriate updates and information to keep the JSC apprised of the progress of the Schedule.

14.7. Joint Project Team Responsibilities.

The JPT's primary responsibilities shall include, but shall not be limited to, the following functions or roles:

(a) serving as technical lead and principal point of contact for all matters related to the Schedule;

(b) overseeing project planning and execution, reporting progress and coordinating all Activities related to the Schedule;

(c) recommending updates to the Schedule including tactics and risk mitigation to the JSC;

(d) leading meetings (at least [**]) to facilitate review and coordinated interpretation of data, information sharing, and timeline monitoring;

(e) preparing for any substantive correspondence, communications or meetings with Governmental Authorities and coordinating with the JSC with respect to the strategy for such correspondence, communications or meetings

(f) facilitating issue resolution at the JPT level and escalating issues to the JSC;

(g) discussing completion of milestones, decision points and Deliverables set forth in each Schedule;

(h) discussing proposed amendments to the Schedule, including the scope of the development activities and budget, and submitting such amendments to JSC for approval;

(i) facilitating coordinated interpretation of data;

(j) facilitating the transfer of information and data and coordination of processes related to the development, Commercialization and Regulatory Approval process;

(k) determining the strategy for any substantive correspondence, communications or meetings with Governmental Authorities; and

(l) oversight of clinical affairs Activities.

14.8. Joint Commercialization Committee.

No later than [**] prior to the anticipated date on which the first Regulatory Approval of a SYROS Product is expected, the Parties will form a joint commercialization team (the "**Joint Commercialization Committee**" or "**JCC**"). The JCC will (as considered reasonable by each Party, in its sole discretion and to the extent legally allowed), discuss a coordinated approach for the sales and marketing of the QIAGEN IVD for use with the SYROS Product. Such JCC shall be constituted and shall operate as the JSC determines and as may be outlined in the relevant Schedule.

14.9. Joint Commercialization Committee Responsibilities.

The JCC's primary responsibilities shall include, but shall not be limited to, the following functions or roles:

(a) facilitating the transfer of information and data and coordination of processes related to the Commercialization of the QIAGEN IVD and the SYROS Product process;

(b) coordination of planned marketing and Commercialization activities , including but not limited to launch strategies for the Markets, field force activities, marketing strategies, alignment of package inserts, instructions for use, data sheets, marketing material, publications, training activities, reimbursement strategies, sharing of market research information and use of advisory boards/key opinion leaders;

(c) preparation and review of each Commercialization Activities Schedule prior to submission for review and approval by the JSC;

(d) forecasting and measuring sales and distribution data to ensure adequate supply of the QIAGEN IVD in each Market; and

(e) oversight of medical affairs Activities.

15. Termination

15.1. Termination by Either Party for Cause; Termination by SYROS for Convenience.

(a) Either Party may terminate this Agreement if the other party commits a material breach of its obligations hereunder; *provided,* that the non-breaching Party provides written notice of such breach to the breaching party and such breach is not cured within thirty (30) days of such notice. For clarity, a breach that is specific to a Project shall not serve to terminate this Agreement, but shall be addressed as set forth below.

(b) Either Party may terminate a Schedule upon thirty (30) days' notice if the other party commits a material breach of the Schedule and fails to cure such breach within the thirty (30) day notice period.

(c) Either Party may terminate this Agreement and any Schedules immediately by written notice to the other Party, if the other Party makes or has made an assignment for the benefit of creditors, is the subject of proceedings in voluntary or involuntary bankruptcy instituted on behalf of or against it (except for involuntary bankruptcies which are dismissed within ninety (90) days) or has a receiver or trustee appointed for substantially all of its property.

(d) Either Party may terminate a Schedule as contemplated in Section 3.3 (Scope Changes) or 9.6(c) (Licenses relevant to Biomarkers).

(e) SYROS may terminate this Agreement and/or any Schedule at any time, with or without cause, upon ninety (90) days' prior written notice to QIAGEN.

15.2. Effects of Termination by SYROS.

(a) In the event of any termination by SYROS under Section 15.1, with regard to the terminated Project(s):

(i) the Parties shall promptly meet to prepare a close-out Schedule,

(ii) SYROS shall make a final payment to QIAGEN for: (A) a pro rata portion of any future milestones toward which work was properly performed prior to the date of the termination notice; (B) any project-specific inventory of the QIAGEN IVD maintained in accordance with this Agreement; and (C) any Pass-through Costs and Expenses that were already paid, or ordered and unable to be cancelled without penalty (and for which such non-cancellable commitments were reasonably made) by QIAGEN pursuant to the Schedule or as otherwise authorized by SYROS, provided that QIAGEN shall provide to SYROS documentation evidencing to SYROS' reasonable satisfaction that such costs were already paid, or are uncancellable without penalty;

(iii) any licenses to Project-Related Background Intellectual Property and, subject to Section 15.2(a)(iv), Foreground Intellectual Property, granted by either Party under this Agreement shall terminate upon the effective date of such termination. For clarification, the licenses to Project Data under Section 8.1 shall survive any expiration or termination of this Agreement or a Project; and

(iv) In the event of termination of this Agreement by SYROS pursuant to Section 15.1[**], all licenses to QIAGEN Foreground IP shall survive any termination or expiration of this Agreement.

(b) In the event of termination by SYROS pursuant to Section 15.1[**], in addition to any effects of termination set forth in Section 15.2(a)(i)-(iii), SYROS shall reimburse QIAGEN's costs in winding down the Project and reallocating employees, which shall be calculated as follows: An amount equal to the number of QIAGEN personnel who were actively engaged in performing Activities in support of the Project at the time of termination, multiplied by the percentage of their time allocated to the Project at that time, multiplied by the Daily FTE Rate (defined below) for the period of Business Days from the date of notice of termination until the date the QIAGEN personnel are reallocated to other activities or projects, not to exceed [**]. QIAGEN will provide SYROS with documentation of Project hours worked by FTEs to evidence such amounts. The Daily FTE Rate shall mean USD $[**] for 2022, and shall increase by [**]% annually thereafter.

15.3. Effects of Termination by QIAGEN.

(a) In the event of a termination by QIAGEN under Section 15.1, with regard to the terminated Project(s):

(i) the Parties shall promptly meet to prepare a close-out Schedule,

(ii) SYROS shall make a final payment to QIAGEN for: (A) a pro rata portion of any future milestones toward which work was properly performed prior to the date of the termination notice; (B) any project-specific inventory of the QIAGEN IVD maintained in accordance with this Agreement; and (C) any Pass-through Costs and Expenses that were already paid, or ordered and unable to be cancelled, without penalty (and for which such non-cancellable commitments were reasonably made) by QIAGEN pursuant to the Schedule or as otherwise authorized by SYROS provided that QIAGEN shall provide to SYROS documentation evidencing to SYROS' reasonable satisfaction that such costs were already paid, or are uncancellable without penalty.

(iii) any intellectual property licenses granted by either Party under this Agreement shall terminate upon the effective date of such termination.

(iv) SYROS shall reimburse QIAGEN's costs in winding down the Project and reallocating employees, which shall be calculated as follows: An amount equal to the number of QIAGEN personnel who were actively engaged in performing Activities in support of the Project at the time of termination, multiplied by the percentage of their time allocated to the Project at that time, multiplied by a daily FTE rate of US $[**] for the period of Business Days from the date of notice of termination until the date the QIAGEN personnel are reallocated to other activities or projects, not to exceed.

15.4. Return of Materials and Confidential Information. At the earlier of completion or termination of a particular Project (or this Agreement as a whole), and except as otherwise permitted herein, each Party shall destroy, or return at the other Party's expense and election, Materials and Confidential Information of the other Party. A Party may retain one copy of Confidential Information of the other Party for the purpose of evidence. The return or destruction of Materials and Confidential Information will not affect the receiving Party´s obligation to observe the confidentiality and non-use restrictions set out in this Agreement. The provisions of this Section 15.4 shall not apply to copies of electronically exchanged Confidential Information made as a matter of routine information

technology backup and to Confidential Information or copies thereof which must be stored by the receiving Party according to provisions of Applicable Law.

15.5. Survival. Termination or expiration of this Agreement will not relieve either Party of any liability which accrued hereunder prior to the effective date of such termination, nor preclude either Party from pursuing all rights and remedies it may have hereunder at law or in equity with respect to any breach of this Agreement, nor prejudice either Party's right to obtain performance of any obligation arising hereunder. Sections 3.1 [Exclusivity] (to the extent included in a Schedule), 4 [Materials and Records], 6 [Payment], 7 [Confidentiality], 8.[Data], 9 Intellectual Property, 15.4 [Return of Materials and Confidential Information], 15.5 [Survival], 16 [Warranties and Disclaimers], 15.2 – 15.4 [Termination], 16.4(c) [Compliance], 17 [Indemnification, Liability and Insurance] and 18 [Miscellaneous], shall survive any termination or expiration of this Agreement. In addition, any other provisions which by their nature are understood to survive the termination or expiration of this Agreement shall so survive.

16. Warranties and Disclaimers

16.1. General Warranties. Each Party hereby represents and warrants to the other Party as of the Effective Date that: (i) it is a corporation duly organized, validly existing, and in good standing under applicable laws, rules and regulations, (ii) it has obtained all necessary consents, approvals and authorizations of all Governmental Authorities (both inside and outside the Markets) and other persons required to be obtained by it in connection with this Agreement, (iii) the execution, delivery and performance of this Agreement have been duly authorized by all necessary corporate action on its part, (iv) it has, to its knowledge, the right to grant the applicable rights and licenses provided for under this Agreement, (v) it and its Affiliates and Representatives performing Activities under this Agreement shall at all times during the Term maintain appropriate licenses, permits, approvals and certifications necessary to lawfully perform its obligations hereunder, and (vi) any biological materials provided by it or on its behalf pursuant to this Agreement for use in connection with the Activities shall be collected or shall have been collected, handled, and transferred in compliance with all Applicable Law, including federal, state, and foreign laws and regulations relating to protection of human research subjects, privacy and security of individually identifiable health information, and standards for notification of breaches of individually identifiable health information applicable in effect at the time and location of the collection and transfer of such

material or information and any applicable policies of any institutional review board, privacy board, or ethics committee with jurisdiction over the collection, handling, and transfer of such material or information.

16.2. No Inconsistent Agreements. Each Party hereby represents, warrants and covenants to the other Party that during the Term it will not grant or convey to any third party any right, license or interest in any Intellectual Property that is inconsistent with the rights and licenses expressly granted to the other Party under this Agreement with respect to the relevant Project.

16.3. No Debarment or Prohibited Payments. Each Party hereby certifies that it will not employ or otherwise use and has not employed or used in any capacity the services of any person (i) debarred by, or (ii) to the best of the respective Party's knowledge, currently subject to a debarment procedure by US Food and Drug Administration (FDA) under Title 21 United States Code Section 335a or any other competent authority in performing any Activities under this Agreement. Each Party further represents and warrants that in connection with the subject matter of this Agreement: (i) none of its employees, agents, officers or directors is a Foreign Official as defined in the U.S. Foreign Corrupt Practices Act, (ii) it will not make, accept or request any payment, either directly or indirectly, of money or other assets to any third party where such payment would constitute violation of any law, including the U.S. Foreign Corrupt Practices Act and the UK Bribery Act 2010, (iii) regardless of legality, it shall neither make, accept nor request any such payment for the purpose of improperly influencing the decisions or actions of any third party, and (iv) it shall report any suspected or actual violation of this Section 16.3 to the other Party upon becoming aware of the same.

16.4. Compliance.

(a) Each Party shall perform all work performed as part of the contractual relationship with the other Party in a manner consistent with all Applicable Law, including, but not limited to, all applicable anti-bribery and antitrust laws. To the extent related to this Agreement, each Party represents and warrants that it has not made or provided, and will not make or provide, any payment or benefit, directly or indirectly, to government officials, customers, business partners, healthcare professionals or any other person in order to secure an improper benefit or unfair business advantage, affect private or official decision-making, affect prescription behaviour, or induce someone to breach professional duties or standards.

(b) Each Party will immediately report to the other Party in writing any suspected or detected violation of the above principles in connection with the other Party's business and, in such cases, will cooperate fully with the other Party in reviewing the matter.

(c) During the Term and for the [**] period following the termination or expiration of this Agreement, each Party through a mutually agreeable, independent third-party auditor, upon reasonable advance notice to and at the auditing Party's sole expense, shall have the right during normal business hours to examine and review such books, records, and other documents and materials, except individual salary information, for the sole purpose of verifying whether the other Party has complied with the compliance obligations stated in this Section 14.

16.5. Disclaimers. THE REPRESENTATIONS AND WARRANTIES SET FORTH ABOVE ARE IN LIEU OF ANY AND ALL OTHER WARRANTIES AND REPRESENTATIONS, EXPRESS, IMPLIED, OR STATUTORY, AND EACH PARTY HEREBY DISCLAIMS ANY AND ALL WARRANTIES OR REPRESENTATIONS, EXPRESS, IMPLIED OR STATUTORY, INCLUDING ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR FOR NON-INFRINGEMENT OF A PATENT, TRADEMARK OR OTHER INTELLECTUAL PROPERTY RIGHTS.

17. Indemnification, Liability and Insurance

17.1. Indemnification by QIAGEN. QIAGEN shall defend, indemnify and hold harmless each of SYROS, its Affiliates and their respective directors, officers, employees and agents, together with the successors and assigns of any of the foregoing (each, a "SYROS Indemnitee") from and against any and all third party claims, suits, actions, demands or judgments (collectively, "Claims") and any and all resultant liabilities, damages, settlements, penalties, fines, costs or expenses (including reasonable attorneys' fees) ("Liabilities") to the extent that such Claims and Liabilities arise out of or in connection with (i) a QIAGEN Indemnitee's negligence or wilful misconduct; (ii) a QIAGEN Indemnitee's violation of Applicable Law; (iii) personal injury or death caused by defective design or manufacture of the Clinical Trial Assay or QIAGEN IVD hereunder, (iv) the breach of any covenant, representation or warranty of QIAGEN contained in this Agreement, (v) the infringement or misappropriation of any Intellectual Property right of a third party as a result of the development, manufacture or Commercialization of any QIAGEN IVD (excluding to the extent resulting from:

(x) the SYROS Biomarker, or (y) Third Party Biomarker IP for which QIAGEN has not assumed responsibility pursuant to a Schedule), and (vi) the infringement or misappropriation of any Third Party Biomarker IP for which QIAGEN has assumed responsibility pursuant to a Schedule; provided, however, that QIAGEN's obligations under this Section 17.1 shall be excused to the extent that such Liabilities arise out of a Claim to which aQIAGEN Indemnitee is entitled to indemnification under Section 17.2.

17.2. Indemnification by SYROS. SYROS shall defend, indemnify and hold harmless each of QIAGEN, its Affiliates, and each of its and their respective directors, officers, employees and agents, together with the successors and assigns of any of the foregoing (each, a "QIAGEN Indemnitee") from and against any and all Claims and Liabilities to the extent arising out of or in connection with (i) a SYROS Indemnitee's negligence or wilful misconduct; (ii) a SYROS Indemnitee's violation of Applicable Law; (iii) personal injury or death caused by the defective design or manufacture of a SYROS Product, (iv) personal injury or death to a Clinical Trial subject resulting from use or administration of a SYROS Product, (v) the breach of any covenant, representation or warranty of SYROS contained in this Agreement, (vi) the infringement or misappropriation of any Intellectual Property right of a third party caused by a SYROS Biomarker, (vii) the infringement or misappropriation of any Intellectual Property right of a third party as a result of the development, manufacture or Commercialization of any SYROS Product (excluding to the extent resulting from Third Party Biomarker IP for which QIAGEN has assumed responsibility pursuant to a Schedule), and (viii) the infringement or misappropriation of any Third Party Biomarker IP other than that for which QIAGEN has assumed responsibility pursuant to a Schedule; provided, however, that SYROS's obligations under this Section 17.2 shall be excused to the extent that such Liabilities arise out of a Claim to which a SYROS Indemnitee is entitled to indemnification under Section 17 .1.

17.3. Indemnification Procedure. A party seeking indemnification or reimbursement hereunder shall give the other party prompt written notice of any such claim or law suit (including a copy thereof) served upon it and shall fully cooperate with the indemnifying party and its legal representatives, at the indemnifying party's expense, in the investigation and defense of any matter the subject of indemnification. The indemnifying party shall have full control over the proceedings, including but not limited to, selection of counsel reasonably acceptable to the indemnified party to tender appearance for the indemnifying party and for the indemnified party. Each party shall consider any reasonable request by the other party to enter into a joint defense or similar agreement, the

form of which shall be reasonably acceptable to both parties. The party seeking indemnification shall not unreasonably withhold its approval of the settlement of any claim, liability, or action covered by Section 17.1 or 17.2, as applicable, will cooperate with counsel of the indemnifying or reimbursing party, and reserves the right to engage its own counsel to assist in the defense at its own expense.

17.4. Neither Party may enter into any settlement, consent judgment or other voluntary final disposition of any Claim and/or Liability for which an Indemnitee seeks indemnification hereunder without the prior written consent of the other Party, such consent not to be unreasonably withheld.

17.5. Limitation of Damages. EXCEPT WITH RESPECT TO LIABILITIES OWED TO THIRD PARTIES PURSUANT TO EACH PARTY'S INDEMNIFICATION OBLIGATIONS UNDER THIS SECTION 17 OR A BREACH OF ITS CONFIDENTIALITY OBLIGATIONS UNDER SECTION 7, NEITHER PARTY WILL BE LIABLE TO THE OTHER FOR ANY INDIRECT, INCIDENTAL, CONSEQUENTIAL, SPECIAL, EXEMPLARY, PUNITIVE, MULTIPLE OR OTHER SIMILAR DAMAGES (INCLUDING ANY CLAIMS FOR LOST PROFITS OR REVENUES) ARISING FROM OR RELATING TO THIS AGREEMENT; PROVIDED, HOWEVER, THAT THIS SHALL NOT LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF EITHER PARTY WITH RESPECT TO ANY THIRD PARTY CLAIMS UNDER THIS ARTICLE 17.

17.6. Insurance. During the Term and until completion of the last Project conducted under this Agreement, each Party shall maintain a comprehensive commercial general liability insurance program, including product liability insurance with coverage limits not less than US$[**] for each occurrence and in the aggregate. SYROS also will maintain clinical trials liability coverage with limits not less than US$[**] for each occurrence and in the aggregate [**]. All insurers utilized to provide coverage required hereunder shall be rated A, Class VII or better by A.M. Best Company in a form satisfactory to both Parties. Upon request, each Party will provide to the other Party respective insurance certificates. For clarification, the insurance coverage required herein may be provided through any reasonable structure of local and global insurance programs.

18. Miscellaneous

18.1. Force Majeure. Neither Party shall be liable for failure or delay in performance under this Agreement due to causes such as an act of God, strike, lockout or other labor dispute, civil commotion, sabotage, fire, flood, explosion, acts of any government, any other similar causes not within the reasonable control of the

Party affected (a "**Force Majeure Event**"). In the event either Party is unable to perform any of its obligations hereunder due to a Force Majeure Event, such Party shall promptly notify the other Party. Performance hereunder shall be promptly resumed after the applicable Force Majeure Event has been remedied. QIAGEN may terminate in writing to the extent affected any Development Project and SYROS may terminate in writing to the extent affected this Agreement or any Schedule .

18.2. Notices. All notices under this Agreement shall be in writing and shall be sent by registered or certified mail, postage prepaid, or by overnight courier service, to the attention of the Legal Department at the addresses of the respective Parties set forth in the first paragraph of this Agreement .

To Syros:

Chief Development Officer
Syros Pharmaceuticals, Inc.
35 CambridgePark Drive
Cambridge, MA 02140

with copy to:
Legal Department
Syros Pharmaceuticals, Inc.
35 CambridgePark Drive
Cambridge, MA 02140

To QIAGEN:

QIAGEN
Attention: Legal Department
19300 Germantown Road
Germantown, MD 20874

18.3. Governing Law and Disputes.

(a) Law. The formation, existence, performance, validity and all aspects of this Agreement shall be governed by and construed in all respects in accordance with the laws of the State of Delaware without regard to its rules on conflicts of laws .

(b) Dispute Resolution. Prior to arbitration, the Parties shall seek informal resolution of disputes. The process shall be initiated with written notice of one Party to the other, describing the dispute with reasonable particularity followed with a written response within [**] of receipt of notice. If a dispute cannot be resolved within [**] after good faith efforts by the Parties, or in the case of disputes submitted to the JSC for resolution pursuant to Section 14.5, within

[**] following the meeting of the Senior Executives, either Party may proceed to binding arbitration without recourse to the ordinary courts of law according the American Arbitration Association, Commercial Arbitration Rules (the "Rules"). For any matter submitted to arbitration pursuant to this Section 18.3(b), the seat of arbitration shall be New York, New York. The number of arbitrators shall be three (3). The arbitrators shall be appointed in accordance with the Rules. The language to be used in the arbitration proceedings shall be English. If any arbitration is brought for the enforcement of this Agreement, or because of any alleged dispute, breach, default or misrepresentation in connection with any of the provisions of this Agreement, the successful or prevailing Party shall be entitled to recover reasonable attorneys' fees and other costs incurred therein, in addition to any other relief to which it or they may be entitled. Notwithstanding anything to the contrary in this Section 18.3, if either Party in its sole judgment believes that any breach of this Agreement could cause it irreparable harm, such Party (i) will be entitled to seek equitable relief in order to avoid such irreparable harm, and (ii) will not be required to follow the procedures set forth in this Section 18.3 with respect to seeking such relief.

18.4. Entire Agreement. This Agreement sets out the entire agreement and understanding between the Parties regarding the subject matter of this Agreement and supersedes all prior discussions, arrangements and agreements, whether oral or in writing or which may be inferred from the conduct of the Parties, including without limitation the Interim Agreement for Feasibility and Proof-of-Concept dated as of [**], as amended, between the Parties .

18.5. Validity/Severability . The invalidity or unenforceability of any provision of this Agreement shall not affect the validity or enforceability of any other provision which shall remain in full force and effect. The Parties undertake to replace such invalid or unenforceable provision by a valid and enforceable provision which accomplishes as far as possible the purpose and the intent of the invalid or unenforceable provision.

18.6. Assignment. This Agreement may not be assigned or otherwise transferred by either Party without the prior written consent of the other Party; *provided*, *however*, that either Party may, without such consent, but upon written notice, assign its rights and obligations under this Agreement in connection with a merger, consolidation or similar transaction or the sale of all or substantially all of the business or assets to which this Agreement relates; and *provided*, *further*, that either Party may, without such consent, but upon written notice, assign its rights and obligations under this Agreement in whole or in part to any Affiliate.

Any purported assignment or transfer in violation of this Section 18.5 shall be void ab initio. This Agreement shall be binding on the P arties and their respective successors and permitted assigns.

18.7. Waiver; Modification of Agreement . No waiver, amendment, or modification of any of the terms of this Agreement shall be valid unless in writing and signed by authorized representatives of both Parties. Failure by either Party to enforce any rights under this Agreement shall not be construed as a waiver of such rights nor shall a waiver by either Party in one or more instances be construed as constituting a continuing waiver or as a waiver in other instances. Any amendments to this Agreement shall be made in writing; the same applies for any waiver or amendment of this written form clause.

18.8. Relationship of the Parties. The relationship of the Parties is that of independent contractors.

18.9. Independent Development. Unless expressly specified otherwise in a Schedule as contemplated in Section 3.1(b), nothing in this Agreement will be construed as restricting either Party's ability to acquire, license, develop, manufacture or distribute for itself, or have others acquire, license, develop, manufacture or distribute for such Party, similar technology performing the same or similar functions as the technology contemplated by this Agreement, or to market and distribute such similar technology in addition to, or in lieu of, the technology contemplated by this Agreement, provided, however, that such activities of such Party comply with all provisions herein.

18.10. Counterparts and Signatures. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original and all of which will together be deemed to constitute one agreement. The Parties agree that the execution of this Agreement by exchanging pdf signatures, and/or by industry standard electronic signature software, shall have the same legal force and effect as the exchange of original signatures. In any proceeding arising under or relating to this Agreement, each Party hereby waives any right to raise any defense or waiver based upon execution of this Agreement by means of such electronic signatures or maintenance of the executed agreement electronically.

IN WITNESS WHEREOF, QIAGEN and SYROS, intending to be legally bound, have executed this Agreement at the dates indicated below by their respective duly authorized representatives.

SYROS PHARMACEUTICALS, INC.

By:/s/ Nancy Simonian

Name: Nancy Simonian
Title: CEO

Date: 3/7/2022

QIAGEN Manchester Limited

By:/s/ Thierry Bernard

Name: Thierry Bernard
Title: Chief Executive Officer

Date: March 4, 2022

SCHEDULE 1

Between Syros Pharmaceuticals, Inc.
35 Cambridge Park Drive
4th Floor
Cambridge, MA 02140, USA
hereinafter **"SYROS"**

and QIAGEN Manchester Limited
Citylabs 2.0
200 Hathersage Road
Manchester
M13 0BH, UK

WHEREAS:

A. SYROS is a biopharmaceutical company engaged in the research and development of products for the treatment of human diseases and conditions, including cancer, and has identified a biomarker that indicates whether a patient is likely to benefit from treatment with SYROS' product tamibarotene (formerly SY-1425); and

B. SYROS has used a clinical trial assay developed by a third party to select patients for inclusion in early clinical trials of the SYROS Product and desires to collaborate with QIAGEN to develop, seek regulatory approval for and commercialize a companion diagnostic for use with the SYROS Product defined below; and

C. SYROS and QIAGEN are parties to an Interim Agreement for Feasibility and Proof-of-Concept entered into as of [**], as amended (the "**Interim Agreement**"), pursuant to which QIAGEN and SYROS have collaborated in the performance of certain activities relating to feasibility, proof-of-concept studies and development activities for *in vitro* diagnostic assay for use with the SYROS Product defined below; and

D. SYROS and QIAGEN have executed a Master Collaboration Agreement (the "**MCA**") dated March 7, 2022 to establish a legal framework for the development of companion diagnostics for SYROS Products; and

E. SYROS wishes to have QIAGEN continue to develop a companion diagnostic and seek regulatory approval for and commercialize a QIAGEN IVD for use with the SYROS Product defined below in the Markets, as defined below (the "**Project**"); and

NOW, therefore, the Parties agree as follows:

1. Definitions.

1.1. All capitalized terms used in this Schedule are either defined below or in the MCA. If a term is defined in the MCA, the definition below shall be considered a further expansion of the definition for the purposes of this Schedule only.

"Control" or "Controlled" or "Controlling" shall mean, with respect to a pharmaceutical product or any item of Intellectual Property, (i) the holding of an investigational new drug application for such pharmaceutical product or (ii) the possession (other than by operation of the MCA or this Schedule) of the right, whether directly or indirectly, and whether by ownership, license or otherwise, to assign, or grant the other Party access or a license or sublicense to such Intellectual Property, as applicable, without violating the terms of any agreement or other arrangement with a third party.

"IVD kit" shall mean the QIAGEN IVD, provided in kit format, being developed under this Schedule, which will be commercially available after FDA approves both the NDA (new drug application) for tamibarotene (SY-1425) and the PMA (pre-market application) for the QIAGEN IVD.

"Markets" shall mean the United States and any additional countries or territories where the Parties mutually agree by an amendment to this Schedule to jointly Commercialize (or have Commercialized) the SYROS Product and the QIAGEN IVD. The Parties acknowledge and agree that upon the request of SYROS, this Schedule will be amended by the Parties to include some or all of the following countries and territories as Markets, subject to the inclusion of mutually agreed milestones and associated payments and costs relating to Commercialization of the QIAGEN IVD in such additional Markets: Canada, the United Kingdom, the member states of the European Economic Area, Switzerland, Mexico, Australia, Russia, Israel and Brazil.

"QIAGEN Biomarker" is not applicable to this Project Plan.

"SYROS Biomarker" shall mean [**].

"**SYROS Product**" shall mean any pharmaceutical product containing tamibarotene as an active ingredient, including any product containing tamibarotene as a sole active ingredient or in combination with one or more other active ingredients, in any dosage form, formulation or presentation, and any improvements to any of the foregoing products.

"**Project Plan**" shall mean the planned Activities for the Project as referred to within this Schedule and detailed within Appendix 1.

2. Effective Date.

This Project Schedule 1 shall be effective as of March 7, 2022.

3. Scope of Work.

Appendix 1 (Project Plan) hereto sets forth the development and related activities to be performed by QIAGEN and SYROS in connection with the development of the Companion Diagnostic for the SYROS Product. QIAGEN shall not (and shall cause its Affiliates not to) initiate any stage, phase or milestone described in this Schedule (and its Appendices) (or the Activities contemplated herein) without SYROS's express written consent, provided that SYROS hereby consents [**].

4. Exclusivity.

During the Term of this Schedule and until [**], other than pursuant to this Agreement or as otherwise approved by SYROS or stated in the following sentence, and in consideration of the mutual promises and covenants of the Parties contained herein and in the MCA, the receipt and sufficiency of which are hereby acknowledged, QIAGEN, on behalf of itself and its Affiliates, will not, directly or indirectly, develop (or grant any license or other rights to any Affiliate or third party to develop) any Clinical Trial Assay or IVD for use with [**] that requires [**]. Notwithstanding anything in this Section 4 or elsewhere in the MCA or this Schedule to the contrary, QIAGEN shall be free to work with sublicensees of SYROS on the development of any IVD or Clinical Trial Assay for use with a SYROS Product.

5. Materials.

SYROS shall without undue delay, provide certain Materials free of charge to QIAGEN for use in the Project, as listed in the Pass Through Costs in **Appendix 1** to this Schedule.

6. Use of Third-Party Contractors

Those Third-Party subcontractors currently agreed by the Parties are set forth in **Appendix 1**. The Contract Laboratories currently agreed by the parties are also set forth in **Appendix 1**.

7. Payments.

7.1 Milestone Fees. SYROS shall pay QIAGEN for achievement of milestones as set forth in **Appendix 1** of this Schedule.

7.2 Pass-through Costs and Expenses. Certain costs and expenses, set forth in Appendix 1 to this Schedule, shall also be reimbursed by SYROS in accordance with Section 6.2 of the MCA. The incurrence of any additional Pass-through Costs and Expenses must be approved in advance by SYROS.

7.3 Purchase Order; Invoicing. Upon execution of this Schedule, SYROS shall promptly issue a purchase order to QIAGEN covering the Milestones, Pass-Through Costs and ongoing costs set forth in the Work Plan, and QIAGEN shall invoice SYROS against such purchase order in accordance with Section 6.1(c) of the MCA. QIAGEN shall invoice SYROS Pass-through Costs and Expenses as provided in the MCA. Invoices can be sent via email to [**].

8. Intellectual Property.

8.1 Background IP. The Parties have compiled a list of all Background Intellectual Property known to be licensed under Section 9 of the MCA, and this list is set forth in Appendix 2. For clarification, neither Party shall be required to disclose the terms of any licenses, but may generally refer to Intellectual Property for which it has a license.

8.2 Third Party Biomarker IP.
(a) Third Party Biomarker IP Licenses. SYROS, at its sole expense, shall obtain and maintain any licenses or other rights to access or use any third-party Intellectual Property for the development or use of the SYROS Biomarker which, but for a license to such Intellectual Property, would be infringed by the performance by SYROS or QIAGEN of Activities pursuant to this Schedule.

9. Term and Effects of Termination.

The Term of this Project Schedule shall commence on the Schedule Effective Date and continue until the completion of all activities and obligations hereunder, unless sooner terminated by either Party under the terms of the MCA.

10. Warranties.

Each party represents and warrants that, as of the Schedule Effective Date, (i) to its knowledge, it owns or Controls all Intellectual Property or other such rights necessary to perform its obligations under the Project in accordance with the MCA and the Schedule; and (ii) it has not received any notice of infringement or any written communication relating to a possible infringement of any Third Party Intellectual Property by its activities prior to the Schedule Effective Date; and (iii) there is no pending litigation relating to a possible infringement of any Third Party Intellectual Property by its Activities prior to the Schedule Effective Date.

11. Entire Agreement.

This Schedule, together with the MCA, sets out the entire agreement and understanding between the Parties regarding the subject matter of this Schedule and supersedes all prior discussions, arrangements, and agreements, whether oral or in writing or which may be inferred from the conduct of the Parties.

12. Conflicts between Schedule and MCA.

This Schedule is incorporated into and made a part of the MCA and the terms and conditions of the MCA shall govern, unless this Schedule specifically and expressly supersedes the MCA on a specific matter and then only with respect to this particular Schedule and the matter so specified.

{Signatures follow on the next page}

IN WITNESS WHEREOF, QIAGEN and SYROS, intending to be legally bound, have executed this Project Schedule 1 by their respective duly authorized representatives.

Syros Pharmaceuticals, Inc.	**QIAGEN Manchester Limited**
By: /s/ Nancy Simonian	By: /s/ Thierry Bernard
Name: Nancy Simonian Title: CEO	Name: Thierry Bernard Title: Chief Executive Officer
Date: 3/7/2022	Date: March 4, 2022

Appendix 1

SYROS Responsibilities

In relation to the development of the IUO assay and the IVD kit, subject to and without limiting the terms and conditions of the MCA, SYROS shall be responsible for the following:

- SYROS shall be solely responsible for the clinical testing for tamibarotene (formerly SY-1425) using the clinical trial assay.
- SYROS shall provide QIAGEN with clinical data, including sample and patient demographic data regarding the use of the IUO assay, as well as patient outcome data to the extent such data is available and necessary, as reasonably determined by QIAGEN, for QIAGEN regulatory filings for the QIAGEN IVD kit and for planning further development activities at QIAGEN under Project Schedule 1.
- SYROS will support the selection of the vendor(s) for the [**]. SYROS will participate in the oversight and management of the vendor(s).
- SYROS and QIAGEN will make reasonable efforts to provide the clinical samples necessary for QIAGEN's verification/validation activities for the IVD kit.

QIAGEN Responsibilities

Subject to and without limiting the terms and conditions of the MCA, QIAGEN shall be responsible for the development of the QIAGEN IVD kit as follows:

- QIAGEN shall lead the development and submission of an IDE (if required) and PMA submission with FDA's Center for Devices and Radiological Health (CDRH) for the QIAGEN IVD kit.
- QIAGEN will contract to establish [**] external sites in addition to QIAGEN's laboratory for the [**]. QIAGEN will be responsible for the oversight, selection, training and qualification of the vendor(s). These costs include BIMO inspections of these sites.
- QIAGEN shall inform and coordinate with SYROS on CDRH-related matters and support SYROS in discussions with FDA's Center for Drug Evaluation and Research (CDER) for tamibarotene all in accordance with and to the extent required by the MCA.
- Subject to the involvement of SYROS described above, QIAGEN shall be responsible for the design, development, and regulatory approval of the QIAGEN IVD kit, including the development of suitable and necessary protocols, in accordance with this Project Schedule 1.
- QIAGEN shall be responsible for manufacturing, supply, and delivery of the QIAGEN IUO assay, including all components, and subject to any intellectual property considerations set forth in section 9, in accordance with and as required by the MCA.

- QIAGEN shall be responsible for preparation of the PMA documentation and laboratory site readiness, as required for submission of the PMA for the IVD kit, in accordance with and as required by the MCA.

MILESTONES AND FEES FOR THE DEVELOPMENT OF THE IPSOGEN RARA RGQ RT-PCR GENE EXPRESSION COMPANION DIAGNOSTIC FOR tamibarotene

QIAGEN will use Commercially Reasonable Efforts to expedite the Activities below with the goal of accelerating the project timelines.

MS	Description	Completion Date (Est)	Payment (USD)
5*	**Transfer & Prototype Batch Manufacture** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
6	**As required: CDRH Pre-Submission; Request for Feedback on Diagnostic Strategy** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
7	**Ipsogen RARA RGQ RT-PCR gene expression CDx Performance Studies Complete:** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
8	**Assay Software Available** [**] Evidence of Milestone Achievement; [**].	[**]	[**]
9	**Clinical Preparation** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
10	**Ethics Approval** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
11	**Pilot Verification Batch Manufacture** [**] Evidence of Milestone Achievement: [**].	[**]	[**]

12	**Initiation of Assay Stability Studies** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
13	**Completion of Reproducibility Studies** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
14	**Completion of Verification** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
15	**Design Output & Design Verification Lock** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
16	**PMA Module 1 Submission – Software and Hardware Verification and Validation to CDRH.** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
17	**Completion of Lab Set-up for the [**] study** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
18	**Analytical Accuracy Reference Method** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
19	**[**] study management and Statistical Analysis Report Generation** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
20	**Completion of Formal Design Review for Design Validation Lock (Completion of Clinical Sample Testing)** [**] Evidence of Milestone Achievement: [**]	[**]	[**]

21	**PMA Module 2 Submission – Analytical Verification and Non-Clinical Studies to CDRH.** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
22	**PMA Module 3 Submission – Manufacturing & Design Controls** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
23	**Bioresearch Monitoring (BIMO) Amendment** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
24	**PMA Module 4 Submission - Clinical Module Preparation and submission** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
25	**US FDA PMA Approval** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
26	**Production Implementation US;** [**] Evidence of Milestone Achievement: [**]	[**]	[**]
Total Milestones for PMA (excluding pass through and on-going costs)			[**]

Please note: International registrations can be included by mutual agreement.

* Milestones 1-4 were contracted via the Interim Agreement.

Appendix 1: Pass Through Costs

Name	Description	Estimated Payment (USD)
Research Grade and GMP Raw materials	[**]	[**]
Cell Lines & Donor Blood	[**]	[**]
Control oligos	[**]	[**]
[**] 3rd Party Development Work	[**]	[**]
[**] 3rd Party Consumables	[**]	[**]
Sample Costs	[**]	[**]
Third party Laboratory costs for [**] studies	[**]	[**]
FDA fees	Fees associated with FDA filing presumed to be as a PMA. https://www.fdahelp.us/fda-fees.html	[**]
Travel	Travel costs associated with training at Testing Lab(s) and in-person meetings.	[**]
Post-Approval study requirements	Should FDA require additional studies as post approval marketing commitments these costs will be passed through to Syros.	[**]
	Estimated Total PTC not to exceed	[**]

Costs presented in the above table reflect an estimate of materials required for the activities listed in this Project Schedule.

On-going costs

Name	Description	Payment (USD)
IUO Tests	QIAGEN will supply IUO tests to clinical testing labs as forecasted and required for test site qualification and for on-going clinical testing of samples.	[**]
Sample Preparation Reagents	QIAGEN will supply sample preparation reagents to clinical testing labs as forecasted to accompany the [**].	[**]
Clinical Test Site Monitoring	During the course of the [**] study, monitoring of the test site(s) and operators carrying out blood based testing will be conducted. The JPT will agree a frequency as required	[**]

The above table reflects an estimate of the ongoing costs associated with the clinical validation of the [**].
Should additional materials be required beyond the scope of this Schedule an amendment to this Schedule will be required to procure the material and the additional costs will be passed onto Syros.

Appendix 2 – SYROS Background Intellectual Property

[**]

Exhibit 31.1

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

I, Nancy Simonian, certify that:

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

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

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

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

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

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

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

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

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

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

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

Syros Pharmaceuticals, Inc.

/s/ Nancy Simonian, M.D.

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

Dated: May 16, 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: May 16, 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 March 31, 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: May 16, 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 March 31, 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: May 16, 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.