UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2022

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

Commission File Number 001-37566

SYNLOGIC, INC.
(Exact name of Registrant as specified in its Charter)

Delaware **(State or other jurisdiction of incorporation or organization)**	**26-1824804** **(I.R.S. Employer Identification No.)**
301 Binney St., Suite 402 **Cambridge, MA** **(Address of principal executive offices)**	**02142** **(Zip Code)**

(617) 401-9975
(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol	Name of exchange on which registered
Common Stock, par value $0.001 per share	SYBX	The Nasdaq Capital 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 ☒

As of November 3, 2022, there were 70,519,940 shares of the registrant's common stock, par value $0.001 per share, outstanding.

FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained herein are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the success of our research and development efforts;
- the initiation, progress, timing, costs and results of clinical trials for our product candidates;
- the time and costs involved in obtaining regulatory approvals for our product candidates;
- the success of our collaborations with third parties;
- the progress, timing and costs involved in developing manufacturing processes and in manufacturing products, as well as agreements with third-party manufacturers;
- the rate of progress and cost of our commercialization activities;
- the expenses we incur in marketing and selling our product candidates, if approved;
- the revenue generated by sales of our product candidates, if approved;
- the emergence of competing or complementary technological developments;
- the terms and timing of any additional collaborative, licensing or other arrangements that we may establish;
- the acquisition of businesses, products and technologies;
- our need to implement additional infrastructure and internal systems;
- our need to add personnel and financial and management information systems to support our product development and potential future commercialization efforts, and to enable us to operate as a public company;
- the development of major public health concerns, including the novel coronavirus outbreak or other pandemics arising globally, and the current and future impact of it and COVID-19, or geopolitical tensions, such as the armed conflict between Russia and Ukraine, on our clinical trials, business operations and funding requirements; and
- other risks and uncertainties, including those listed under Part II, Item 1A. "Risk Factors".

Any forward-looking statements in this Quarterly Report on Form 10-Q reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Part II, Item 1A. "Risk Factors" and elsewhere in this Quarterly Report on Form 10-Q. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Quarterly Report on Form 10-Q also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

SYNLOGIC, INC.

QUARTERLY REPORT ON FORM 10-Q

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SYNLOGIC, INC. AND SUBSIDIARIES

Unaudited Consolidated Balance Sheets

(In thousands, except share amounts)

	September 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 15,622	$ 16,438
Short-term marketable securities	76,034	112,150
Accounts receivable	1,500	—
Prepaid expenses and other current assets	4,302	4,721
Total current assets	97,458	133,309
Long-term marketable securities	—	8,041
Property and equipment, net	7,901	9,088
Right of use asset - operating lease	14,240	13,889
Restricted cash	1,097	1,097
Prepaid research and development, net of current portion	7,529	9,309
Other assets	12	3
Total assets	$ 128,237	$ 174,736
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,718	$ 1,944
Accrued expenses	4,770	4,402
Deferred revenue	971	531
Lease liability - operating lease	4,130	3,191
Finance lease obligations	13	12
Total current liabilities	11,602	10,080
Long-term liabilities:		
Lease liability - operating lease, net of current portion	16,199	17,372
Finance lease obligations, net of current portion	8	18
Total long-term liabilities	16,207	17,390
Commitments and contingencies (Note 11)		
Stockholders' equity		
Common stock, $0.001 par value		
250,000,000 shares authorized as of September 30, 2022 and December 31, 2021. 70,285,495 shares issued and outstanding as of September 30, 2022 and 69,698,844 shares issued and outstanding as of December 31, 2021.	70	70
Additional paid-in capital	441,072	438,113
Accumulated other comprehensive loss	(391)	(45)
Accumulated deficit	(340,323)	(290,872)
Total stockholders' equity	100,428	147,266
Total liabilities and stockholders' equity	$ 128,237	$ 174,736

The accompanying notes are an integral part of the unaudited consolidated financial statements.

SYNLOGIC, INC. AND SUBSIDIARIES

Unaudited Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except share and per share amounts)

	For the Three Months Ended		For the Nine Months Ended	
	September 30, 2022	September 30, 2021	September 30, 2022	September 30, 2021
Revenue	$ 678	$ 916	$ 1,074	$ 1,162
Operating expenses:				
Research and development	14,610	13,355	38,405	35,254
General and administrative	4,402	3,616	12,785	11,528
Total operating expenses	19,012	16,971	51,190	46,782
Loss from operations	(18,334)	(16,055)	(50,116)	(45,620)
Other income (expense):				
Interest and investment income	422	41	658	151
Interest expense	(1)	(1)	(3)	(2)
Other income (expense)	1	(1)	10	(1)
Total other income, net	422	39	665	148
Net loss	$ (17,912)	$ (16,016)	$ (49,451)	$ (45,472)
Net loss per share - basic and diluted	$ (0.25)	$ (0.29)	$ (0.69)	$ (0.91)
Weighted-average common stock outstanding - basic and diluted	72,108,113	55,336,936	72,061,935	49,730,231
Comprehensive loss:				
Net loss	$ (17,912)	$ (16,016)	$ (49,451)	$ (45,472)
Net unrealized (loss) gain on marketable securities	42	(2)	(346)	(5)
Comprehensive loss	$ (17,870)	$ (16,018)	$ (49,797)	$ (45,477)

The accompanying notes are an integral part of the unaudited consolidated financial statements.

SYNLOGIC, INC. AND SUBSIDIARIES

Unaudited Consolidated Statements of Stockholders' Equity

(In thousands, except share amounts)

	Common stock $0.001 par value		Additional paid-in	Accumulated other comprehensive	Accumulated	Total
	Shares	Amount	capital	income (loss)	deficit	equity
			For the Three Months Ended September 30, 2022			
Balance at June 30, 2022	70,230,235	$ 70	$ 440,124	$ (433)	$ (322,411)	$ 117,350
Issuance of common stock under employee stock purchase plan	66,139	—	54	—	—	54
Cancellation of restricted stock	(10,879)	—	—	—	—	—
Equity-based compensation expense	—	—	894	—	—	894
Unrealized gain (loss) on securities	—	—	—	42	—	42
Net loss	—	—	—	—	(17,912)	(17,912)
Balance at September 30, 2022	70,285,495	$ 70	$ 441,072	$ (391)	$ (340,323)	$ 100,428
			For the Three Months Ended September 30, 2021			
Balance at June 30, 2021	52,375,344	$ 52	$ 387,782	$ 11	$ (259,767)	$ 128,078
Proceeds from issuance of common stock, net of issuance costs	17,250,000	18	48,426	—	—	48,444
Exercise of options	93,033	—	209	—	—	209
Issuance of common stock under employee stock purchase plan	23,592	—	61	—	—	61
Cancellation of restricted stock	(34,428)	—	—	—	—	—
Equity-based compensation expense	—	—	808	—	—	808
Unrealized gain (loss) on securities	—	—	—	(2)	—	(2)
Net loss	—	—	—	—	(16,016)	(16,016)
Balance at September 30, 2021	69,707,541	$ 70	$ 437,286	$ 9	$ (275,783)	$ 161,582
			For the Nine Months Ended September 30, 2022			
Balance at December 31, 2021	69,698,844	$ 70	$ 438,113	$ (45)	$ (290,872)	$ 147,266
Exercise of options	35,562	—	61	—	—	61
Issuance of restricted stock	507,260	—	—	—	—	—
Issuance of common stock under employee stock purchase plan	106,629	—	137	—	—	137
Cancellation of restricted stock	(62,800)	—	—	—	—	—
Equity-based compensation expense	—	—	2,761	—	—	2,761
Unrealized gain (loss) on securities	—	—	—	(346)	—	(346)
Net loss	—	—	—	—	(49,451)	(49,451)
Balance at September 30, 2022	70,285,495	$ 70	$ 441,072	$ (391)	$ (340,323)	$ 100,428
			For the Nine Months Ended September 30, 2021			
Balance at December 31, 2020	38,183,273	$ 38	$ 345,394	$ 14	$ (230,311)	$ 115,135
Proceeds from issuance of common stock in connection with ATM offering, net of issuance costs	2,447,211	3	8,047	—	—	8,050
Proceeds from issuance of common stock, net of issuance costs	28,750,000	29	80,990	—	—	81,019
Exercise of options	125,146	—	273	—	—	273
Issuance of restricted stock	242,454	—	—	—	—	—
Issuance of common stock under employee stock purchase plan	42,653	—	94	—	—	94
Restricted stock awards withheld for payment of employees' withholding tax liability	(18,187)	—	(73)	—	—	(73)
Cancellation of restricted stock	(65,009)	—	—	—	—	—
Equity-based compensation expense	—	—	2,561	—	—	2,561
Unrealized gain (loss) on securities	—	—	—	(5)	—	(5)
Net loss	—	—	—	—	(45,472)	(45,472)
Balance at September 30, 2021	69,707,541	$ 70	$ 437,286	$ 9	$ (275,783)	$ 161,582

The accompanying notes are an integral part of the unaudited consolidated financial statements.

SYNLOGIC, INC. AND SUBSIDIARIES

Unaudited Consolidated Statements of Cash Flows

(In thousands)

	Nine Months Ended September 30, 2022	Nine Months Ended September 30, 2021
Cash flows from operating activities:		
Net loss	$ (49,451)	$ (45,472)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	1,907	1,832
Equity-based compensation expense	2,761	2,561
Accretion/amortization of investment securities	(364)	243
Change in carrying amount of operating lease right of use asset	2,347	1,532
Changes in operating assets and liabilities:		
Accounts receivable	(1,500)	(1,000)
Prepaid expenses and other current assets	419	854
Prepaid research and development, net of current portion	1,780	840
Accounts payable and accrued expenses	107	455
Deferred revenue	440	988
Operating lease liabilities	(2,932)	(1,968)
Other assets	(9)	(3)
Net cash used in operating activities	(44,495)	(39,138)
Cash flows from investing activities:		
Purchases of marketable securities	(66,191)	(97,981)
Proceeds from maturity of marketable securities	110,366	77,272
Proceeds from redemption of marketable securities	—	1,270
Purchases of property and equipment	(685)	(507)
Net cash provided by (used in) investing activities	43,490	(19,946)
Cash flows from financing activities:		
Payments on finance lease obligations	(9)	(6)
Proceeds from issuance of common stock, net of issuance costs	—	81,167
Proceeds from issuance of common stock in connection with at-the-market offering, net of issuance costs	—	8,047
Proceeds from employee stock purchases and exercise of stock options	198	367
Payment of employee withholding taxes relating to restricted stock awards	—	(73)
Net cash provided by financing activities	189	89,502
Net increase (decrease) in cash, cash equivalents and restricted cash	(816)	30,418
Cash, cash equivalents and restricted cash at beginning of period	17,535	33,604
Cash, cash equivalents and restricted cash at end of period	$ 16,719	$ 64,022
Supplemental disclosure of non-cash investing activities:		
Assets acquired under operating lease obligation	$ 2,698	$ 460
Property and equipment purchases included in accounts payable and accrued expenses	$ 35	$ 138
Supplemental disclosure of non-cash financing activities:		
Purchase under finance lease	$ —	$ 36
Issuance costs included in accounts payable and accrued expenses	$ —	$ 145
Cash paid for interest	$ 2	$ 1

The accompanying notes are an integral part of the unaudited consolidated financial statements.

(1) Nature of Business

Organization

Synlogic, Inc., together with its wholly owned and consolidated subsidiaries ("Synlogic" or "the Company"), is a clinical-stage biopharmaceutical company applying synthetic biology to the discovery and development of Synthetic Biotics. Synthetic Biotics are generated from Synlogic's proprietary platform, leveraging a reproducible, modular approach to the generation of novel drug candidates that perform or deliver critical therapeutic functions. Synthetic Biotics are designed to metabolize a toxic substance, compensate for missing or damaged metabolic pathways or deliver combinations of therapeutic factors. Synlogic's goal is to discover, develop and ultimately commercialize Synthetic Biotics. Since incorporation, the Company has devoted substantially all of its efforts to the research and development of its product candidates.

Risks and Uncertainties

At September 30, 2022, the Company had approximately $91.7 million in cash, cash equivalents, and short-term marketable securities, $1.1 million of restricted cash and an accumulated deficit of approximately $340.3 million. Since its inception through September 30, 2022, the Company has primarily financed its operations through the issuance of preferred stock, units and warrants, the sale of its common stock, collaborations, including with Roche, and cash received in the Merger (defined below). In the absence of positive cash flows from operations, the Company is highly dependent on its ability to find additional sources of funding in the form of debt or equity financing. Management believes that the Company has sufficient cash to fund its operations through at least twelve months from the issuance of these financial statements.

As an early-stage company, the Company is subject to a number of risks common to other life science companies, including, but not limited to, raising additional capital, development by its competitors of new technological innovations, risk of failure in preclinical and clinical studies, safety and efficacy of its product candidates in clinical trials, the risk of relying on external parties such as contract research organizations (CROs) and contract manufacturing organizations (CMOs), the regulatory approval process, market acceptance of the Company's products once approved, lack of marketing and sales history, dependence on key personnel and protection of proprietary technology. The Company's therapeutic programs are currently pre-commercial, spanning discovery through development and will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval, prior to commercialization of any product candidates. These efforts require significant amounts of additional capital, adequate personnel, infrastructure, and extensive compliance-reporting capabilities. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained, that any products developed will obtain necessary regulatory approval or that any approved products will be commercially viable. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate revenue from product sales. The Company may never achieve profitability, and unless and until it does, it will continue to need to raise additional capital or obtain financing from other sources, such as strategic collaborations or alliances.

COVID-19

While the Company is not aware of a material impact from the continuation of the COVID-19 pandemic through September 30, 2022, the full extent to which the COVID-19 pandemic will directly or indirectly impact the Company's business, results of operations, and financial condition, including expenses and manufacturing, clinical trials, and research and development costs, depends on future developments that are uncertain at this time.

(2) Summary of Significant Accounting Policies

The significant accounting policies described in the Company's audited financial statements as of and for the year ended December 31, 2021, and the notes thereto, which are included in the Company's Annual Report on Form 10-K for the year ended December 31, 2021, filed with the Securities and Exchange Commission (SEC) on March 17, 2022 (the 2021 Annual Report), have had no material changes during the three and nine months ended September 30, 2022.

Basis of Presentation

The accompanying consolidated financial statements and the related disclosures as of September 30, 2022 and for the three and nine months ended September 30, 2022 and 2021 are unaudited and have been prepared in accordance with accounting principles generally accepted in the United States (GAAP) and the rules and regulations of the SEC for interim financial statements. Accordingly, they do not include all of the information and notes required by GAAP for complete financial statements. These interim consolidated financial statements should be read in conjunction with the Company's 2021 and 2020 audited consolidated financial statements and notes included in the 2021 Annual Report. The consolidated balance sheet as of December 31, 2021 included herein was derived from the audited financial statements as of that date but does not include all disclosures including notes required by GAAP for complete financial statements. In the opinion of management, the unaudited interim consolidated financial statements reflect all adjustments, consisting of normal and recurring adjustments, necessary for the fair presentation of the Company's financial position and results of operations for the three and nine months ended September 30, 2022 and 2021. The results of operations for the interim periods are not necessarily indicative of the results to be expected for the year ending December 31, 2022 or any other interim period or future year or period.

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Synlogic and its wholly owned subsidiaries. All intercompany accounts and transactions have been eliminated in consolidation.

Recently Issued Accounting Pronouncements

New accounting pronouncements are issued by the FASB from time to time, and rules are issued by the SEC that the Company has or will adopt as of a specified date. Unless otherwise noted, management does not believe that any recently issued accounting pronouncements issued by the FASB or guidance issued by the SEC had, or is expected to have, a material impact on the Company's present or future financial statements.

(3) Fair Value of Financial Instruments

The tables below present information about the Company's assets that are measured at fair value on a recurring basis and indicate the fair value hierarchy of the valuation techniques the Company utilized to determine such fair value, as described under Note 2*, Summary of Significant Accounting Policies,* in the audited financial statements included in the 2021 Annual Report.

The Company's investment portfolio includes many fixed income securities that do not always trade on a daily basis. As a result, the pricing services used by the Company applied other available information as applicable through processes such as benchmark yields, benchmarking of like securities, sector groupings and matrix pricing to prepare evaluations. In addition, model processes were used to assess interest rate impact and develop prepayment scenarios. These models take into consideration relevant credit information, perceived market movements, sector news and economic events. The inputs into these models may include benchmark yields, reported trades, broker-dealer quotes, issuer spreads and other relevant data.

At September 30, 2022 and December 31, 2021, the Company has classified assets measured at fair value on a recurring basis as follows (in thousands):

		Fair Value Measurements at Reporting Date Using		
Description	September 30, 2022	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds	$ 13,627	$ 13,627	$ —	$ —
Commercial paper (included in cash and cash equivalents)	1,995	—	1,995	—
Commercial paper	56,758	—	56,758	—
Corporate debt securities	—	—	—	—
U.S. government agency securities and treasuries	19,276	19,276	—	—
Total	$ 91,656	$ 32,903	$ 58,753	$ —

		Fair Value Measurements at Reporting Date Using		
Description	December 31, 2021	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds	$ 16,437	$ 16,437	$ —	$ —
Commercial paper	106,277	—	106,277	—
Corporate debt securities	5,873	—	5,873	—
U.S. government agency securities and treasuries	8,041	8,041	—	—
Total	$ 136,628	$ 24,478	$ 112,150	$ —

Cash equivalents, prepaid expenses and other current assets, accounts payable and accrued expenses at September 30, 2022 and December 31, 2021 are carried at amounts that approximate fair value due to their short-term maturities. Finance lease obligations at September 30, 2022 and December 31, 2021 approximate fair value as they bear interest at a rate approximating a market interest rate.

(4) Available-for-Sale Investments

The following tables summarize the available-for-sale securities held at September 30, 2022 and December 31, 2021 (in thousands):

September 30, 2022	Amortized cost	Gross unrealized gains	Gross unrealized losses	Fair Value
Commercial paper	$ 56,943	$ —	$ (185)	$ 56,758
Corporate debt securities	—	—	—	—
U.S. government agency securities and treasuries	19,482	—	(206)	19,276
Total	$ 76,425	$ —	$ (391)	$ 76,034

December 31, 2021	Amortized cost	Gross unrealized gains	Gross unrealized losses	Fair Value
Commercial paper	$ 106,298	$ 8	$ (29)	$ 106,277
Corporate debt securities	5,876	—	(3)	5,873
U.S. government agency securities and treasuries	8,062	—	(21)	8,041
Total	$ 120,236	$ 8	$ (53)	$ 120,191

The contractual maturity of all securities held at September 30, 2022 was eight months or less. There were 28 and 20 investments in an unrealized loss position at September 30, 2022 and December 31, 2021, respectively, none of which had been in an unrealized loss position for more than twelve months. The aggregate fair value of the securities in an unrealized loss position at September 30, 2022 and December 31, 2021 was $76.0 million and $72.2 million, respectively. The Company reviews its investments for other-than-temporary impairment whenever the fair value of an investment is less than amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. To determine whether an impairment is other-than-temporary, the Company considers whether it has the ability and intent to hold the investment until a market price recovery and considers whether evidence indicating the cost of the investment is recoverable outweighs evidence to the contrary. The Company did not hold any securities with an other-than-temporary impairment at September 30, 2022.

Gross realized gains and losses on the sales of investments have not been material to the Company's consolidated statement of operations.

(5) Property and Equipment, net

Property and equipment, net consists of the following (in thousands):

	September 30, 2022	December 31, 2021
Laboratory equipment	$ 9,263	$ 8,274
Computer and office equipment	793	756
Furniture and fixtures	500	500
Leasehold improvements	9,820	9,561
Construction in progress	52	623
	20,428	19,714
Less accumulated depreciation	(12,527)	(10,626)
Property and equipment, net	$ 7,901	$ 9,088

(6) Accrued Expenses

Accrued expenses consist of the following (in thousands):

	September 30, 2022	December 31, 2021
Payroll related	$ 2,960	$ 3,495
Professional fees	471	298
Research and development	999	336
Other	340	273
Total accrued expenses	$ 4,770	$ 4,402

(7) Stockholders' Equity

In June 2019, the Company issued to Ginkgo Bioworks, Inc. (Ginkgo) an aggregate of 6,340,771 shares of common stock at a purchase price per share of $9.00, and pre-funded warrants (the Pre-Funded Warrants) to purchase an aggregate of 2,548,117 shares of common stock at an exercise price of $9.00 per share, with $8.99 of such exercise price paid at the closing of the offering. The net proceeds to the Company were approximately $79.9 million. None of the Pre-Funded Warrants have been exercised as of September 30, 2022. (See Note 9, *Collaboration Agreements*: *Ginkgo Collaboration*).

The Company had a previous sales agreement with Cowen and Company, LLC (Cowen) with respect to an at-the-market (ATM) offering program, which was entered into on October 13, 2017. In an ATM offering, exchange-listed companies incrementally sell newly issued shares into the secondary trading market through a designated broker-dealer at prevailing market prices. During the three months ended March 31, 2021, 2,447,211 shares of common stock were sold pursuant to the ATM, resulting in net proceeds of approximately $8.1 million. There were no sales pursuant to the Cowen ATM subsequent to March 31, 2021.

In July 2021, the Company entered into a new sales agreement with Jefferies, LLC (Jefferies) with respect to an ATM offering program, under which the Company may offer and sell, from time to time at its sole discretion, shares of its common stock having aggregate sales proceeds of up to $50.0 million. Jefferies is not required to sell any specific amount but acts as the Company's sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. During the nine months ended September 30, 2022, no shares of common stock were sold pursuant to the sales agreement with Jefferies.

The Company has reserved for future issuance the following shares of common stock related to the potential exercise of Pre-Funded Warrants, exercise of stock options, and the employee stock purchase plan:

	September 30, 2022
Common stock issuable under pre-funded warrants	2,548,117
Options exercisable to purchase common stock	3,028,542
Employee Stock Purchase Plan	—
Total	5,576,659

(8) Equity-based Compensation

On January 1, 2022, the number of shares of common stock available for issuance under the 2015 Equity Incentive Award Plan (the "2015 Plan") and the 2015 Employee Stock Purchase Plan ("ESPP") was increased by 3,484,942 shares and 696,988 shares, respectively, due to the annual evergreen provision to increase shares available under the 2015 Plan and the ESPP. As of September 30, 2022, there were an aggregate of 1,824,645 shares available for future grant under the 2017 Stock Incentive Plan (the "2017 Plan") and the 2015 Plan, and 1,275,200 shares available for future grant under the ESPP.

The following table summarizes equity-based compensation expense within the Company's consolidated statements of operations and comprehensive loss for the three and nine months ended September 30, 2022 and 2021 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Research and development	$ 390	$ 319	$ 1,143	$ 1,093
General and administrative	504	489	1,618	1,468
	$ 894	$ 808	$ 2,761	$ 2,561

The following table summarizes equity-based compensation expense by type of award for the three and nine months ended September 30, 2022 and 2021 (in thousands):

	Three Months Ended September 30		Nine Months Ended September 30,	
	2022	2021	2022	2021
Stock options	$ 764	$ 744	$ 2,429	$ 2,243
Restricted stock awards	111	50	277	284
ESPP	19	14	55	34
	$ 894	$ 808	$ 2,761	$ 2,561

During the nine months ended September 30, 2022, the Company granted 3,440,399 stock options with a weighted average exercise price of $1.70. As of September 30, 2022, there was $6.1 million of unrecognized share-based compensation related to unvested stock option grants which is expected to be recognized over a weighted average period of 2.71 years. The total unrecognized share-based compensation cost will be adjusted for actual forfeitures as they occur.

During the nine months ended September 30, 2022, the Company granted 507,260 restricted stock awards with a weighted average grant date fair value per share of $1.97. As of September 30, 2022, there was approximately $1.3 million of unrecognized share-based compensation related to restricted stock awards granted, which is expected to be recognized over a weighted average period of 3.0 years. The total unrecognized share-based compensation cost will be adjusted for actual forfeitures as they occur.

For a full description of the Company's equity plans, refer to Note 9, Equity-based Compensation and Equity Incentive Plans in the 2021 Annual Report.

(9) Collaboration Agreements

Roche Collaboration

In June 2021, the Company entered into a Pilot Collaboration and Option Agreement (the Roche Collaboration and Option Agreement) with F. Hoffmann-La Roche Ltd (Roche Basel) and Hoffmann-La Roche Inc. (Roche US, and together with Roche Basel, Roche). Under the terms of the Roche Collaboration and Option Agreement, the Company and Roche will seek to collaborate to research and pre-clinically develop Synthetic Biotics for addressing an undisclosed novel target for the treatment of inflammatory bowel disease.

During the nine months ended September 30, 2022 and 2021, the Company recognized $1.1 million and $1.2 million, respectively, as collaboration revenue associated with the Roche Collaboration and Option Agreement. During the three months ended September 30, 2022 and 2021, the Company recognized $0.7 million and $0.9 million, respectively, as collaboration revenue associated with the Roche Collaboration and Option Agreement. Deferred revenue from the collaboration amounted to $1.0 million as of September 30, 2022, all of which is included in current liabilities. Additionally, the Company recorded accounts receivable of $1.5 million as of September 30, 2022 as a result of having earned a milestone under the Roche Collaboration and Option Agreement in August 2022.

For a full description of the Roche Collaboration and Option Agreement, refer to Note 10, Collaboration Agreements in the 2021 Annual Report.

Ginkgo Collaboration

In 2017, the Company established a technology collaboration with Ginkgo. In June 2019, the Company expanded its collaboration and entered into an agreement with Ginkgo for the research and development of engineered microbial therapeutic products (See Note 7). Under the 2019 expanded agreement, the Company made a prepayment to Ginkgo of $30.0 million for its foundry services that will be provided to the Company over an initial term of five years. The prepayment of foundry services is recorded in Prepaid expenses and other current assets and Prepaid research and development, net of current portion on the September 30, 2022 consolidated balance sheet. At September 30, 2022, the Company had remaining balances of $1.3 million and $7.5 million of current and non-current prepaid research and development costs related to this transaction, respectively. Upon the expiration of such initial term and, if applicable, an additional period, any portion of the prepayment that has not been used to purchase services from Ginkgo will be retained by Ginkgo.

(10) Net Loss per Share

Basic net loss per share is computed using the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share is computed using the sum of the weighted-average number of shares of common stock outstanding during the period and if dilutive, the weighted-average number of potential shares of common stock, including unvested restricted common stock and outstanding stock options. In June 2019, the Company sold 6,340,771 shares of common stock and Pre-Funded Warrants to purchase an aggregate of 2,548,117 shares of common stock at an exercise price of $9.00 per share, with $8.99 of such exercise price paid at the closing of the offering (see Note 10*, Ginkgo Collaboration,* in the audited financial statements included in the 2021 Annual Report). The shares of common stock into which the warrants may be exercised are considered outstanding for the purposes of computing net loss per share.

The Company's potentially dilutive shares, which include outstanding stock options, unvested restricted common stock and potential shares issuable under the ESPP, are considered to be common share equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

The following potential common shares, presented based on amounts outstanding at each period end, were excluded from the calculation of the diluted net loss per share attributable to common stockholders for the period indicated because including them would have had an anti-dilutive effect.

	As of September 30,	
	2022	2021
Unvested restricted common stock awards	660,071	312,033
Outstanding options to purchase common stock	7,369,534	4,537,618
Potential shares issuable under the ESPP	—	—

(11) Commitments and Contingencies

In the ordinary course of business, the Company may be subject to legal proceedings, claims and litigation as the Company operates in an industry susceptible to patent legal claims. The Company accounts for estimated losses with respect to legal proceedings and claims when such losses are probable and estimable. Legal costs associated with these matters are expensed when incurred. The Company is not currently a party to any material legal proceedings.

The Company's commitments are described in the Company's consolidated financial statements as of and for the year ended December 31, 2021 and the notes thereto included in the Annual Report on Form 10-K filed with the SEC on March 17, 2022. On January 21, 2022, the Company entered into two Statements of Work with Azzur Group, LLC (Azzur). Pursuant to the first of the SOWs (the Third SOW), the Company has agreed to pay Azzur $650,000 to renovate and upgrade the cleanroom space at Azzur for the Company's expanded use. The second of the SOWs (the Fourth SOW) replaces the Second SOW that the Company entered into with Azzur on April 29, 2021. The Fourth SOW extends the term of the lease, for the period beginning January 2022 through March 2023 (the Third Term). The Fourth SOW contains an option to extend the lease. As of September 30, 2022, the Company determined that it was more likely than not to exercise the option to extend the lease. The Third and Fourth SOWs resulted in an adjustment to the operating lease right-of-use asset and corresponding operating lease liabilities of $1.8 million. The total remaining liability associated with the Azzur lease is approximately $2.4 million as of September 30, 2022. For a full description of the Azzur embedded lease, refer to Note 13, *Leases* in the 2021 Annual Report.

(12) Related-Party Transactions

In June 2019, the Company expanded its collaboration and entered into an agreement with Ginkgo for the research and development of engineered microbial therapeutic products. As of September 30, 2022, Ginkgo owned 6,340,771 shares of the Company's outstanding common stock. See Note 10, *Ginkgo Collaboration,* in the audited financial statements included in the 2021 Annual Report.

Under the agreement the Company made a prepayment to Ginkgo of $30.0 million for its foundry services that will be provided to the Company over an initial term of five years. At September 30, 2022, the Company had remaining balances of $1.3 million and $7.5 million of current and non-current prepaid research and development costs related to this transaction, respectively. The Company used $0.7 million and $2.4 million of the prepaid research and development expenses for the three and nine months ended September 30, 2022.

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

Forward-Looking Information

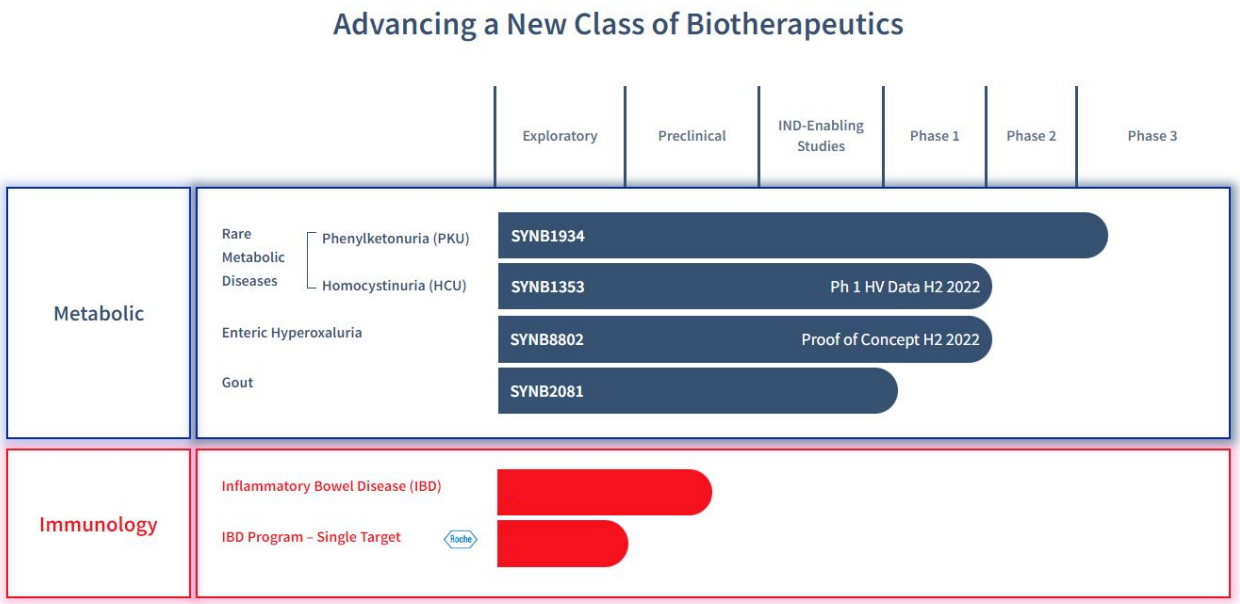
The interim financial statements and this Management's Discussion and Analysis of Financial Condition and Results of Operations should be read together with our audited financial statements and accompanying notes for the year ended December 31, 2021 and 2020 included in our Annual Report on Form 10-K filed with the SEC on March 17, 2022 (the 2021 Annual Report). In addition to historical information, this discussion and analysis contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act). Please see "Risk Factors" beginning on page [27] of this Quarterly Report on Form 10-Q for a discussion of certain risk factors applicable to our business, financial condition, and results of operations. Operating results are not necessarily indicative of results that may occur for the full fiscal year or any other future period. On August 28, 2017, Synlogic, Inc., formerly known as Mirna Therapeutics, Inc. (NASDAQ: MIRN) (Mirna), completed a business combination with Synlogic, a private company, pursuant to the Agreement and Plan of Merger and Reorganization, dated as of May 15, 2017 (the Merger Agreement), pursuant to which the private Synlogic entity survived as a wholly owned subsidiary of Mirna (the Merger). Immediately after completion of the Merger, Mirna changed its name to "Synlogic, Inc." (NASDAQ: SYBX). The term "Private Synlogic" refers to Synlogic Operating Company, Inc. (formerly known as Synlogic, Inc.) prior to the consummation of the Merger. Unless otherwise indicated, references to the terms the "combined company", "Synlogic", the "Company", "we", "our" and "us" refer to Private Synlogic prior to the consummation of the Merger and Synlogic, Inc. (formerly known as Mirna Therapeutics, Inc.) and its subsidiaries upon the consummation of the Merger described herein. The term "Mirna" refers to the Mirna Therapeutics, Inc. and its subsidiaries prior to the Merger.

Business Overview

Synlogic is a clinical-stage biotechnology company advancing a new paradigm of biotherapeutics through its unique and proprietary approach to synthetic biology. Synthetic biology leverages engineering principles to enable the design of new biological systems, genetic circuits and molecular components. Synlogic is delivering the power of synthetic biology to medicine, combining the precision of engineering with rational drug development to develop what are called Synthetic Biotics. Synthetic Biotics are a novel drug modality that uses programmable, precision genetic engineering of well-characterized probiotics to exert localized activity for therapeutic benefit, with a focus on metabolic and immunologic diseases.

Our Drug Candidate Pipeline

Synlogic's pipeline includes its lead program in phenylketonuria (PKU), which has demonstrated proof of concept with plans to start a pivotal, Phase 3 study in the first half of 2023, and additional novel drug candidates designed to treat homocystinuria (HCU), enteric hyperoxaluria and gout. The rapid advancement of these Synthetic Biotics has been enabled by Synlogic's reproducible, target-specific drug design, with a focus on metabolic and immunological diseases. In addition to its clinical programs, Synlogic has a research collaboration with Roche focused on the discovery of a novel Synthetic Biotic for the treatment of inflammatory bowel disease (IBD). Synlogic has also developed two drug candidates through a research collaboration with Ginkgo Bioworks, Inc. (Ginkgo), SYNB1353, designed to consume methionine for the potential treatment of HCU, and SYNB2081, designed to lower uric acid for the potential treatment of gout, as well as additional undisclosed preclinical assets by combining Synlogic's approach to Synthetic Biotics with Ginkgo's Codebase and Foundry services.



Metabolic Disease

There are a number of metabolic diseases involving a lack of certain enzymes that are responsible for metabolizing commonly occurring byproducts of digestion. The absence of these enzymes is caused by either a genetic mutation characterized by a dysfunctional metabolic pathway, such as PKU or HCU, or organ dysfunction, such as enteric hyperoxaluria. In patients with these diseases, the absence of certain enzymes causes metabolites to accumulate to in the gut and systemically throughout the body. In patients with PKU and HCU, these metabolites build up to toxic levels resulting in serious health consequences, including irreversible neurological dysfunction.

PKU

Overview

Our PKU program historically has included two development candidates, SYNB1618 and SYNB1934. We developed both first generation SYNB1618 and the further optimized, next-generation SYNB1934, as orally administered, non-systemically absorbed potential biotherapeutics for the treatment for PKU, a genetic disease caused by inherited mutations that impair the PAH enzyme's ability to metabolize phenylalanine (Phe), an amino acid found in natural protein that can become neurotoxic at high levels and lead to neurocognitive impairments and developmental disorders. The key to risk reduction in PKU is lifelong metabolic control of Phe levels. The PKU population is relatively large for a rare disease, with ~17,000 in the US and more than ~150,000 globally diagnosed due to widespread newborn screening.

Treatment options for PKU are currently limited due to efficacy and safety, and many of those who are treated remain in need of additional Phe-lowering. Our approach focuses on reducing plasma levels of Phe by consuming Phe in the gastrointestinal (GI) tract. Both candidate strains are based on the shared *chassis* of the well-characterized probiotic E. coli Nissle, and were designed as Synthetic Biotics using precision genetic engineering to produce PAL and LAAD, both phe-consuming enzymes. We introduced SYNB1934 as a next generation strain, and it reflects additional optimization of the PAL enzyme specifically for greater Phe consumption. Findings to date support the potential for an efficacious, safe, convenient, and flexible treatment option for PKU that could be used as both a monotherapy for currently untreated patients, as well as an adjunctive treatment option for patients currently taking sapropterin (Kuvan®). SYNB1618 has received both Orphan Drug and Fast Track designations by the US Food and Drug Administration (FDA) and orphan medicinal product designation by the European Medicines Agency.

We have completed enrollment in our Phase 2 study, Synpheny-1, with the objective of evaluating the safety, tolerability, and efficacy of both drug candidates. The study also served to provide confirmation of Phe-consuming activity as expected in PKU patients, and to inform the trial design and dose ramp that are expected for the pivotal Phase 3 study.

The Phase 2 Synpheny-1 study met these objectives, with top-line results including:

- The study enrolled 20 patients with PKU; eleven patients were enrolled in the SYNB1618 arm and nine patients were enrolled in the SYNB1934 arm.
- Both strains demonstrated clinically meaningful reductions on fasting plasma Phe levels. On an “all comers” basis, the day 14 mean change from baseline in fasting plasma Phe was -20% for SYNB1618 and -34% for SYNB1934.
- Results were consistent and positive across all measured indicators of activity for both drug candidates, including plasma D5-Phe, plasma D5-trans-cinnamic acid (TCA); and urinary D5-hippuric acid (HA), with numerically greater changes observed for SYNB1934, consistent with previously shared results in healthy volunteers in our Phase 1 study.
- Results from patients who were already taking sapropterin (Kuvan®) at baseline, and then received SYNB1618 and SYNB1934, were consistent with the overall efficacy profile, demonstrating the potential for adjunctive use.
- All adverse events were mild or moderate in severity, were predominantly gastrointestinal (GI) in nature, and resolved upon cessation of treatment. There were no serious adverse events (SAEs).

The Synpheny-1 Phase 2 Study

The Synpheny-1 study was a Phase 2, open-label, 29-day study to assess safety, tolerability and efficacy in SYNB1618 and SYNB1934 in patients with PKU. The study included a dose-ramp regimen over 15 days of treatment, with days 7 through 14 at the constant dose of $1x10^{12}$live cells. Endpoints included plasma Phe, the biomarker used in the clinical management of PKU and primary endpoint in pivotal studies of previously approved PKU medications.

We also assessed the effectiveness of our approach to consuming Phe through these Synthetic Biotics by reviewing multiple strain-specific biomarkers. An important goal of Synpheny-1 was to confirm proof of concept by demonstrating phe-metabolizing activity in patients with these biomarkers. One assessment included a tracer study in which patients took labeled D5-Phe as part of a test meal followed by a 24-hour collection period. This was done at baseline and after the treatment period to assess the drug’s effect. We also measured two metabolic byproducts which can only be produced if the strains are consuming Phe via the PAL enzyme TCA in plasma and HA in urine. These highly specific biomarkers enabled us to confirm strain activity. Additional endpoints include the incidence of treatment-emergent adverse events (TEAEs). During the study, dietary intake of Phe was carefully managed to match patients’ usual protein and Phe intake to ensure that each patient provided their own internal control.

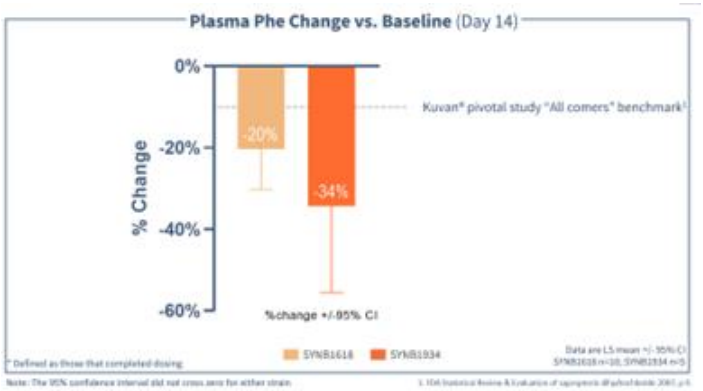
The Phase 2 study was initiated in August 2020, as a single-arm open label study with SYNB1618. Positive interim analysis findings, achieving proof of concept for SYNB1618, were reported in September 2021. In parallel, we shared findings from a Phase 1 study in healthy volunteers with SYNB1934, which included a cohort designed to provide a head-to-head safety bridge with SYNB1618. The Phase 1 study confirmed greater potency in Phe-consuming activity by SYNB1934 in healthy volunteers.

Based on the positive interim analysis with SYNB1618 and the Phase 1 findings with SYNB1934, including the safety bridge with SYNB1618, a second study arm with SYNB1934 was added to the Synpheny-1 Phase 2 study. In addition, the protocol was amended to include patients who were already taking sapropterin (Kuvan®), enabling the ability to obtain data regarding the drug candidates as adjunctive treatments to sapropterin (Kuvan®) as well as monotherapy treatment options.

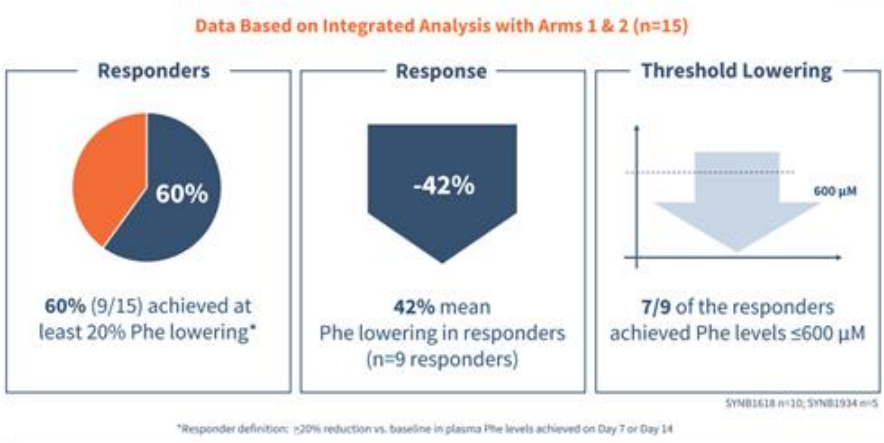
Synpheny-1 enrolled 20 adults with PKU who had Phe levels over 600 micromolar at screening despite existing management, with an average Phe level of approximately 1,000 micromolar. Patient baseline demographics represented a balance of ages and genders, in addition to a range in terms of baseline Phe levels as well as diet and sapropterin (Kuvan®) use, across both arms of the study, that is consistent with the broader population.

Top-Line Efficacy Findings

Results included achieving reductions in levels of fasting plasma Phe from baseline for both strains. On an "all comers" basis, the day 14 mean change from baseline in fasting plasma Phe was -20% for SYNB1618 and -34% for SYNB1934.



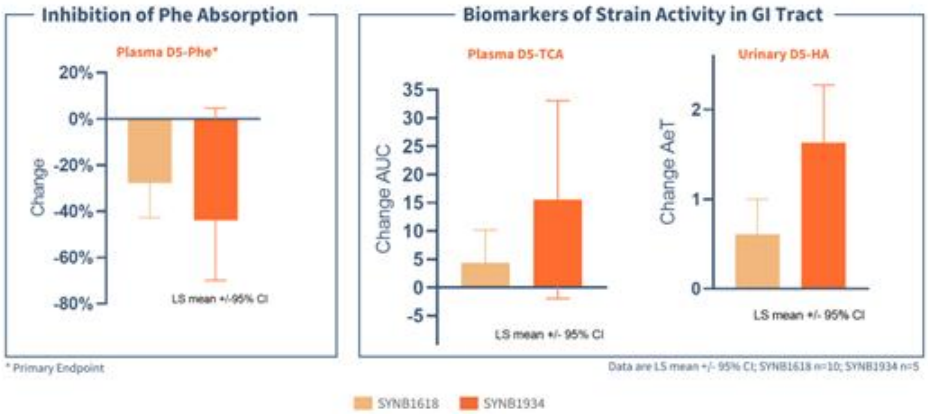
Response was defined as ≥20% reduction in Phe at either day 7 or day 14. Overall, 60% of patients enrolled in the study met these criteria (six of the ten patients dosed with SYNB1618 and three of the five patients that have completed dosing with SYNB1934). Phe reduction for those responders in aggregate averaged 42%.



Among the responders, the ranges for Phe reduction by the strain were 20%-61% and 29%-80% for SYNB1618 and SYNB1934, respectively.

Data includes findings from both SYNB1618 and SYNB1934 when provided as monotherapy or in addition to a treated baseline that included sapropterin (Kuvan®). The results were consistent with the broader efficacy findings. This was expected based on the distinct mechanism of action of these strains, and provides support for advancing into Phase 3 with the goal of a design that would support adjunctive use to sapropterin in addition to monotherapy.

As noted earlier, an important objective of the Phase 2 Synpheny-1 study was to confirm proof of concept in PKU patients by demonstrating the strains' ability to consume Phe as designed, through the GI-restricted mechanism that converts Phe to the metabolic byproducts of TCA and HA. We were able to confirm this activity in both strains, across each measured endpoint. In addition, across each endpoint, we saw indicators of greater potency of SYNB1934. These findings are consistent with those shared last year from the head-to-head healthy volunteer Phase 1 study done with both strains. We now believe we have the additional data needed to advance to Phase 3 in the first half of next year.



Top-Line Safety Summary

Adverse events were all mild to moderate, predominantly GI in nature, and similar across SYNB1618 and SYNB1934. All AEs resolved upon cessation of treatment. There were no SAEs. Across the study, three patients discontinued due to GI-related adverse events, one withdrew consent, and one patient withdrew following an adverse event of facial flushing which was attributed to a possible allergic reaction.

Across the program, we have found GI-related adverse events to be dose-related, and to vary by individual. We have also learned through our ongoing clinical programs with Synthetic Biotics across our platform, that the incidence and severity of these adverse effects can be reduced through the use of a dose-ramp.

For our planned Phase 3 study, we plan on starting at a low dose and on incorporating best practices from probiotic dosing of a slower dose ramp, with extended time at each dose prior to advancing to the next dose. Based on these data and learnings to date, we believe this will improve the dosing experience, and ultimately help more patients benefit from treatment.

Next Steps and Phase 3 Planning

Based on our data to date, we have confirmed that SYNB1934 will be the candidate for the pivotal Phase 3 study we expect to initiate in the first half of 2023. These results are now incorporated into a total of four studies in our clinical development program that includes more than 230 individuals dosed.

Phase 3 study readiness activities are underway, and we have progressed our work on process development and stability, further de-risking the path to potential commercialization from a Chemistry, Manufacturing, and Control (CMC) perspective.

For our planned Phase 3 study, we have the precedents of two FDA-approved therapies, with similar designs. Both were approved based on a primary endpoint of plasma Phe reduction vs. placebo. Based on these precedents and learnings from our own program, we also expect our Phase 3 study to include three parts: Part 1, to identify responders and non-responders using a pre-defined responder definition of greater than or equal to 20% Phe reduction; Part 2, a placebo controlled primary analysis of plasma Phe levels in that responder population; and Part 3, an open-label extension for safety assessment purposes.

As noted above, we expect Part 1 to include a more gradual and extended dose ramp compared to what was used in the Phase 2 study, and we expect to start patients consistently at the lowest dose.

Homocystinuria

HCU is a rare inherited metabolic disorder that affects the metabolism of the amino acid methionine, a protein found in many foods including meat, fish, and dairy products. HCU is caused by a genetic defect which results in the absence of an enzyme known as cystathionine beta-synthase (CBS). When CBS is absent, homocysteine and other toxic chemicals and their byproducts, including methionine, build up in the blood and urine. Elevated homocysteine levels are associated with a multisystem disorder, including impairments of the eye (ectopia lentis and/or severe myopia), skeletal system (excessive height, long limbs, scoliosis, pectus excavatum), vascular system (thromboembolism), and CNS (development delay and intellectual disability).

In November 2021 we announced the nomination of SYNB1353, a novel, orally administered, non-systemically absorbed live biotherapeutic drug candidate engineered to consume methionine in the gastrointestinal (GI) tract thereby lowering an amino acid known as tHcy in HCU patients and potentially allowing an increase in natural protein intake. SYNB1353 was developed as part of a research collaboration with Ginkgo. We hold worldwide development and commercialization rights to SYNB1353. We initiated a Phase 1 clinical trial of SYNB1353 for the treatment of HCU in July 2022 and expect to report Phase 1 trial data in healthy volunteers in the second half of 2022.

Enteric Hyperoxaluria

Enteric hyperoxaluria is an acquired metabolic disorder with no approved treatment options. It is characterized by recurrent kidney stones, caused by increased absorption of dietary oxalate, which is present in many common foods including leafy greens, nuts, and chocolate and results in oxalate deposition and resultant crystal formation in the kidneys. Enteric hyperoxaluria often occurs as a result of a primary insult to the bowel, such as inflammatory bowel disease, short bowel syndrome, or surgical procedures such as Roux-en-Y bariatric weight-loss surgery. The disorder may cause dangerously high levels of urinary oxalate and progressive kidney damage. In May 2020, we announced the nomination of a clinical candidate for enteric hyperoxaluria, SYNB8802. We initiated a Phase 1 clinical trial of SYNB8802 in the fourth quarter of 2020. SYNB8802 is being assessed for safety and tolerability, strain kinetics, changes in plasma and urine biomarkers of strain activity, and the potential to reduce urinary oxalate in the Phase 1 clinical trial. In 2021, Synlogic reported positive proof-of-mechanism for SYNB8802 from a Phase 1b clinical trial that demonstrated lowering of urinary and fecal oxalate levels in healthy volunteers with diet-induced hyperoxaluria. Data from a proof-of-concept trial assessing the lowering of urinary oxalate in patients who have undergone Roux-en-Y gastric bypass surgery is expected in the second half of 2022.

Gout

Gout is a metabolic disease that results in a complex and severe form of inflammatory arthritis that occurs when excess uric acid in the body forms crystals in the joints. Patients experience symptoms such as intense joint pain, inflammation and redness, and limited range of motion in the affected joints. Current treatment options present limitations in both safety and efficacy, highlighting a need for new approaches. In addition, gout is a recognized risk factor in chronic kidney disease. SYNB2081 is a Synthetic Biotic designed to lower uric acid levels systemically by metabolizing uric acid in the GI tract. We believe that this approach offers potential benefits as an orally administered, non-systemically absorbed treatment option to lower systemic levels of uric acid, thereby reducing the burden of gout. We are currently advancing SYNB2081 through IND-enabling studies.

Additional Pipeline Programs in Metabolic & Immunological Diseases

Synthetic Biotics are well-suited for addressing known disease targets that have been associated with validated biological pathways in metabolic and immunological diseases. Building on our progress in metabolic diseases, we are increasingly focusing our research efforts on immunological diseases, such as IBD, where an orally administered, non-systemically absorbed and locally acting mechanism could address medical needs by offering a differentiated product profile and patient experience.

IBD is a group of diseases characterized by significant local inflammation in the GI tract typically driven by T cells, activated macrophages and compromised function of the epithelial barrier. IBD pathogenesis is linked to both genetic and environmental factors and may be caused by altered interactions between gut microbes and the intestinal immune system. Compromised gut barrier function also plays a central role in autoimmune diseases pathogenesis. A single layer of epithelial cells separates the luminal contents of the gut from the host circulatory system and the immune cells in the body. Disrupting the epithelial layer can lead to pathological exposure of foreign antigens from the lumen resulting in increased susceptibility to autoimmune disorders. The interplay between the gut microbiota and the host is thought to play a key role in the maintenance of the epithelial barrier as well as homeostatic immunity. Thus, enhancing barrier function and reducing inflammation in the gastrointestinal tract are potential therapeutic mechanisms for the treatment or prevention of autoimmune disorders. Our Synthetic Biotic platform is designed to allow for the effective programming of *E. coli* Nissle to execute these functions, including the metabolic production of factors such as short chain fatty acids to enhance barrier function, and secreting proteins, such as immunomodulatory cytokines.

Current approaches to treat IBD are focused on therapeutics that modulate the immune system and suppress inflammation. These therapies include steroids, such as prednisone, and tumor necrosis factor inhibitors, such as Humira® (adalimumab). However, these approaches are associated with systemic immunosuppression, which includes greater susceptibility to infectious diseases and cancer. According to the Centers for Disease Control (CDC), in 2015 an estimated three million adults in the United States were reported as being diagnosed with IBD. In June of 2021 we entered into a research collaboration and option agreement with Roche (the Roche Collaboration and Option Agreement) for the discovery of a novel Synthetic Biotic for the treatment of IBD. In addition, we continue to advance additional, wholly-owned preclinical research efforts in IBD. In August 2022, we achieved our second pre-specified research milestone and earned a second milestone payment due under the terms of the Roche Collaboration and Option Agreement.

Among immune conditions, working to treat IBD allows us to leverage knowledge and expertise gained from our oral metabolic programs to develop living medicines that can act locally at the site of disease in the gut. Because our approach is based on local delivery to the site of inflammation and not on systemic administration, we anticipate that our Synthetic Biotics may offer an attractive safety profile in this therapeutic category, where safety is a particularly desirable attribute in a product profile compared to options available today.

We hold all rights to develop IBD Synthetic Biotics for all effectors targeting IBD. This allows us to leverage our expertise in strain engineering, quantitative biology, regulatory, and manufacturing to expand our wholly owned GI-based program portfolio to include IBD. We may enter into strategic alliances in the future to maximize the value of our programs and our Synthetic Biotic platform.

We developed a portfolio of Synthetic Biotics to treat certain cancers which were designed to modify the tumor microenvironment, activate the immune system and result in tumor reduction. These Synthetic Biotics could be used in combination with other cancer therapies such as checkpoint inhibitors. Our Synthetic Biotic clinical immuno-oncology (IO) candidate is SYNB1891, an intratumorally administered Synthetic Biotic medicine engineered to act as a dual innate and adaptive immune activator. On November 10, 2021, we announced that our Phase 1 trial of SYNB1891 in combination with PD-L1 checkpoint inhibitor patients with advanced solid tumors or lymphoma had completed enrollment. No further studies are planned for SYNB1891 and we are focusing our research and development efforts specifically on metabolic and immunological diseases.

We currently operate in one reportable business segment—the discovery and development of Synthetic Biotics. To date, we have dedicated substantially all of our activities to the research and development of our product candidates. We have funded our operations to date primarily with proceeds from the sale of preferred stock, common stock, preferred units, warrants, payments received under the Roche Collaboration and Option agreement, prior collaborations, interest earned on investments, and cash received in the Merger.

We have not generated any revenue to date from product sales and have incurred significant operating losses since our inception. We have incurred net losses of approximately $17.9 million and $49.5 million for the three and nine months ended September 30, 2022, respectively and $16.0 million and $45.5 million for the three and nine months ended September 30, 2021, respectively. As of September 30, 2022, we had an accumulated deficit of approximately $340.3 million, and we expect to incur losses for the foreseeable future as we develop our product candidates. We expect our expenses and capital requirements will increase substantially in connection with our ongoing activities, as we:

- complete preclinical studies, initiate and complete clinical trials for product candidates;
- contract to manufacture product candidates or manufacture product candidates internally;
- advance research and development related activities to expand our product pipeline;

- seek regulatory approval for our product candidates;
- maintain, expand and protect our intellectual property portfolio;
- hire additional staff, including clinical, scientific, commercial, and management personnel;
- expand our existing infrastructure and secure space in a facility to support continued growth in our research and development efforts; and
- add operational and finance personnel to support product development efforts and to support operating as a public company.

We do not expect to generate product revenue unless and until we successfully complete clinical development and obtain regulatory approvals for our product candidates, either alone or in collaboration with third parties. Additionally, we expect to utilize third-party contract research organizations (CROs) and contract manufacturing organizations (CMOs) to carry out our clinical development and manufacturing activities, and we do not yet have a commercial organization. If we obtain regulatory approval for any of our product candidates, we expect to incur significant expenses related to developing our internal commercialization capability to support product sales, marketing and distribution. Accordingly, we anticipate that we will seek to fund our operations through public or private equity or debt financings, collaborations or licenses, finance lease transactions or other available financing transactions. However, we may be unable to raise additional funds through these or other means when needed. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if it will be able to achieve or maintain profitability. Even if we are able to generate product revenue, we may not become profitable.

Impact of the COVID-19 pandemic on our business

The COVID-19 pandemic continues to affect economies and business around the world. The extent and duration of such effects remain uncertain and difficult to predict, particularly as virus variants continue to spread. We are actively monitoring and managing our response and assessing actual and potential impacts to our operating results and financial condition, as well as developments in our business, which could further impact the developments, trends and expectations described below. See the risk factor titled, "A pandemic, epidemic, or outbreak of an infectious disease, such as COVID-19 may materially and adversely affect our business and our financial results." described in "Risk Factors" in Part II, Item 1A, found elsewhere in this Quarterly Report on Form 10-Q.

Effects of Inflation

We do not believe that inflation has had a material impact on our business or operating results during the periods presented. However, inflation, has had, and may continue to have, an impact on the labor costs we incur to attract and retain qualified personnel, costs to conduct clinical trials and other operational costs. Inflationary costs could adversely affect our business, financial condition and results of operations. In addition, increased inflation has had, and may continue to have, an effect on interest rates. Increased interest rates may adversely affect our borrowing rate and our ability to obtain, or the terms under which we can obtain, any potential additional funding.

Financial Overview

Revenue

Revenue for the three and nine months ended September 30, 2022 was generated from the Roche Collaboration and Option Agreement. In June 2021, we announced that we entered into the Roche Collaboration and Option Agreement for the discovery of novel Synthetic Biotics for the treatment of IBD. The collaboration agreement contains multiple deliverables, which include an exclusive option for Roche to negotiate a definitive collaboration and license agreement for further development of the Product Candidate and acquire research and development milestones. See Note 9, *Collaboration Agreements: Roche Collaboration* in the notes to the unaudited consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q for a full discussion of the arrangement.

Research and Development Expense

Research and development expense consists of expenses incurred in connection with the discovery and development of our product candidates, including the conduct of preclinical and clinical studies and product development, which are expensed as they are incurred. These expenses consist primarily of:

- compensation, benefits and other employee related expenses;

- supplies to support our internal research and development efforts;
- research and development related facility and depreciation costs;
- leased manufacturing space; and
- third-party contract costs relating to research, process and formulation development, preclinical and clinical studies and regulatory operations.

The lengthy process of securing regulatory approvals for new drugs requires the expenditure of substantial resources. Any delay or failure to obtain regulatory approvals would materially adversely affect our product candidate development efforts and our business overall. Given the inherent uncertainties of pharmaceutical product development, we cannot estimate with any degree of certainty the likelihood, timing or cost of obtaining regulatory approval and marketing our product candidates and thus, when, if ever, our product candidates will generate revenues and cash flows.

The successful development of our product candidates is highly uncertain and subject to a number of risks. Refer to the risk factors under the heading *Risks Related to the Development of Our Product Candidates* in Part II, Item 1A, found elsewhere in this Quarterly Report on Form 10-Q.

We invest carefully in our pipeline, and the commitment of funding for each subsequent stage of our development programs is dependent upon the receipt of clear, supportive data. We anticipate that we will make determinations as to which additional programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical data of each product candidate, as well as the competitive landscape and ongoing assessments of such product candidate's commercial potential. We expect our research and development costs will be substantial for the foreseeable future. We expect costs associated with our drug development candidates to increase as the programs progress through clinical trials and new programs progress toward IND and into development.

We track direct research and development expenses, consisting principally of external costs, such as costs associated with contract research organizations and manufacturing of preclinical and clinical drug product and other outsourced research and development expenses to specific product programs. Costs related to specific product candidates are tracked upon the selection of a product candidate. We do not allocate employee and consulting-related costs, costs associated with our platform and facility expenses, including depreciation or other indirect costs, to specific product candidate programs because these costs are deployed across multiple product candidate programs under research and development and, as such, are separately classified. The table below summarizes our research and development expenses by categories of costs for the periods presented (in thousands):

	For the Three Months Ended September 30,		For the Nine Months Ended September 30,	
	2022	2021	2022	2021
SYNB1618	$ 1,326	$ 983	$ 2,842	$ 2,995
SYNB1934	1,734	1,776	2,489	2,273
SYNB8802	1,080	2,258	3,138	4,672
SYNB1353	1,207	—	1,477	—
SYNB1891	28	521	482	1,876
External pre-development candidate expenses and unallocated expenses	1,850	1,127	5,822	3,294
Internal research and development expenses	7,385	6,690	22,155	20,144
	$ 14,610	$ 13,355	$ 38,405	$ 35,254

General and Administrative Expense

General and administrative expense consists primarily of compensation, benefits and other employee-related expenses for personnel in our administrative, finance, legal, information technology, investor relations, business development and human resource functions. Other general and administrative costs include the legal costs of pursuing patent protection of our intellectual property, facility and information technology infrastructure costs, directors' and officers' insurance, and professional fees for accounting, tax, legal and consulting services. We anticipate that our general and administrative expenses will increase in the future as we support our continued research and development and potential commercialization of our product candidates. Additionally, if and when we believe a regulatory approval of the first product candidate appears likely, we anticipate an increase in payroll and related expenses as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidates.

Other Income (Expense)

Interest and investment income consists of income earned on investments. Interest expense consists of expense related to our finance leases. Other expense consists primarily of gains and losses on foreign currency invoices.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations is based upon our consolidated financial statements prepared in accordance with generally accepted accounting principles in the U.S. (GAAP). The preparation of these financial statements requires us to make certain estimates and assumptions that affect the reported amounts of assets and liabilities, the reported amounts of revenues and expenses during the reported periods and related disclosures.

Our critical accounting policies are described in our 2021 Annual Report. During the nine months ended September 30, 2022, there were no new or material changes to our existing critical accounting policies. We believe that these identified policies are critical to fully understanding and evaluating our financial condition and results of operations.

Our estimates and assumptions, including those related to revenue recognition and research and development expenses are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. The estimates and assumptions involved in our revenue recognition policy, particularly (a) assessing the number of performance obligations; (b) determination of transaction price; (c) determining the pattern over which performance obligations are satisfied, including estimates to complete performance obligations, and those estimates and assumptions involved in our contract research accrual process, particularly estimates of work completed to date; involve a greater degree of judgment, and therefore we consider revenue recognition and research and development expenses to be our critical accounting policies. We evaluate our estimates and assumptions on an ongoing basis. Actual results may differ from our estimates under different assumptions or conditions.

Results of Operations

The following discussion summarizes the key factors our management believes are necessary for an understanding of our consolidated financial results.

Three Months Ended September 30, 2022 Compared to Three Months Ended September 30, 2021

	For the Three Months Ended		Change
	September 30, 2022	September 30, 2021	$
		(in thousands)	
Revenue	$ 678	$ 916	$ (238)
Operating expenses:			
Research and development	14,610	13,355	1,255
General and administrative	4,402	3,616	786
Total operating expenses	19,012	16,971	2,041
Loss from operations	(18,334)	(16,055)	(2,279)
Other income (expense):			
Interest and investment income	422	41	381
Interest expense	(1)	(1)	0
Other income (expense)	1	(1)	2
Total other income, net	422	39	383
Net loss	$ (17,912)	$ (16,016)	$ (1,896)

Revenue

Revenue was $0.7 million for the three months ended September 30, 2022, as compared to $0.9 million for the three months ended September 30, 2021. The revenue for both periods was related to services performed under the Roche collaboration that we entered into in June 2021.

Operating Expenses

Research and Development Expense

Research and development expense was $14.6 million for the three months ended September 30, 2022 compared to $13.4 million in the corresponding period in 2021. The increase in research and development expense was primarily due to an increase of $1.1 million of clinical development costs for SYNB1353, $0.5 million in professional services, $0.4 million of manufacturing costs, $0.3 million of nonclinical development costs, $0.3 million in research and development support costs, $0.3 million in compensation, benefits and other employee-related expenses and $0.1 million of clinical development costs for SYNB1618. These increases were offset by decreases of $1.2 million of clinical development costs for SYNB8802, $0.4 million of clinical development costs for SYNB1891 and $0.2 million of clinical development costs for SYNB1934.

General and Administrative Expense

General and administrative expense was $4.4 million for the three months ended September 30, 2022, compared to $3.6 million for the corresponding period in 2021.The increase was primarily due to increased compensation, benefits and other employee-related expenses of $0.4 million, increased professional services of $0.3 million and increase support costs of $0.1 million.

Other Income (Expense)

Other income was $0.4 million for the three months ended September 30, 2022, compared to $0.1 million for the corresponding period in 2021. The increase in other income was related to an increase in interest income generated by our investment account.

Nine Months Ended September 30, 2022 Compared to Nine Months Ended September 30, 2021

	For the Nine Months Ended		Change
	September 30, 2022	September 30, 2021	$
	(in thousands)		
Revenue	$ 1,074	$ 1,162	$ (88)
Operating expenses:			
Research and development	38,405	35,254	3,151
General and administrative	12,785	11,528	1,257
Total operating expenses	51,190	46,782	4,408
Loss from operations	(50,116)	(45,620)	(4,496)
Other income (expense):			
Interest and investment income	658	151	507
Interest expense	(3)	(2)	(1)
Other income (expense)	10	(1)	11
Total other income, net	665	148	517
Net loss	$ (49,451)	$ (45,472)	$ (3,979)

Revenue

Revenue was $1.1 million for the nine months ended September 30, 2022, compared to $1.2 million for the nine months ended September 30, 2021. Revenue for both periods was related to services performed under the Roche collaboration that we entered into in June 2021.

Operating Expenses

Research and Development Expense

Research and development expense was $38.4 million for the nine months ended September 30, 2022, compared to $35.3 million in the corresponding period in 2021. The increase in research and development expense was due to increases of $1.3 million of clinical development costs for SYNB1353, $1.2 million in professional services, $1.0 million in research and development support costs, $1.0 million of compensation, benefits and other employee-related expenses, $0.8 million of manufacturing costs, $0.7 million of nonclinical development costs and $0.2 million of clinical development costs for SYNB1618. These increases were partially offset by decreases of $1.6 million of clinical development costs for SYNB8802, $1.3 million of clinical development costs for SYNB1891 and $0.2 million of clinical development costs for SYNB1934.

General and Administrative Expense

General and administrative expense was $12.8 million for the nine months ended September 30, 2022, compared to $11.5 million for the corresponding period in 2021. The increase was primarily due to increased compensation, benefits and other employee-related expenses of $1.0 million and increased professional services of $0.4 million, offset by decreases of support costs of $0.1 million.

Other Income (Expense)

Other income was $0.7 million for the nine months ended September 30, 2022, compared to $0.2 million for the corresponding period in 2021. The increase in other income was related to an increase in interest income generated by our investment account.

Liquidity and Capital Resources

We have incurred losses since our inception on March 14, 2014 and, as of September 30, 2022, we had an accumulated deficit of approximately $340.3 million. We have financed our operations to date primarily through the sale of preferred stock, common stock, preferred units and warrants, payments received under collaboration agreements, including the technology collaboration with Ginkgo, the Roche Collaboration and Option agreement, and prior collaborations, interest earned on investments, and cash received in the Merger. At September 30, 2022, we had approximately $91.7 million in cash, cash equivalents, and short-term marketable securities. Our cash and cash equivalents include amounts held in money market funds, stated at cost plus unrealized gain and loss, which approximates fair market value. Our available-for-sale securities include amounts held in corporate debt securities, commercial paper and U.S. government agency securities and treasuries. We invest cash in excess of immediate requirements in accordance with our investment policy, which limits the amounts we may invest in any one type of investment and requires all investments held by us to maintain minimum ratings from Nationally Recognized Statistical Rating Organizations so as to primarily achieve liquidity and capital preservation.

During the nine months ended September 30, 2022, our cash, cash equivalents and short-term marketable securities balance decreased approximately $44.9 million. This decrease was primarily due to the cash used to operate our business, including payments related to, among other things, research and development and general and administrative expenses as we continue to invest in our primary drug candidates and support the development of our proprietary platform. These decreases were offset by the proceeds from maturity of marketable securities.

The following table sets forth the major sources and uses of cash, cash equivalents and restricted cash for each of the periods below (in thousands):

	Nine Months Ended September 30,	
	2022	2021
	(in thousands)	
Net cash, cash equivalents and restricted cash provided by (used in)		
Operating activities	$ (44,495)	$ (39,138)
Investing activities	43,490	(19,946)
Financing activities	189	89,502
Net increase (decrease) in cash, cash equivalents and restricted cash	$ (816)	$ 30,418

Cash Flows from Operating Activities

Net cash, cash equivalents and restricted cash used in operating activities was approximately $44.5 million for the nine months ended September 30, 2022. The primary use of cash was our net loss of $49.5 million, changes in our assets and liabilities of $1.7 million, partially offset by $6.7 million of non-cash items primarily including depreciation, equity-based compensation, and the right of use asset. The changes in our assets and liabilities include decreases in prepaid research and development expenses, as a result of the work being completed on the Ginkgo collaboration, decreases in the operating lease liability, decreases in prepaid expenses and other current assets, increases in accounts receivable, as a result of having earned a milestone with the Roche collaboration in August 2022, increases in accounts payable and accrued expenses, and increases in deferred revenue.

Net cash, cash equivalents and restricted cash used in operating activities was approximately $39.1 million for the nine months ended September 30, 2021. The primary use of cash was our net loss of $45.5 million, changes in our assets and liabilities of $0.2 million, partially offset by $6.2 million of non-cash items primarily including depreciation, equity-based compensation, and the right of use asset. The changes in our assets and liabilities includes the addition of accounts receivable due to the $1.0 million to be received from Roche for the milestone that was achieved in September 2021, decreases in prepaid research and development expenses, as a result of the work being completed on the Ginkgo collaboration, decreases in prepaid expenses and other current assets, decreases in the operating lease liability, increases in accounts payable and accrued expenses, and increases in deferred revenue.

Cash Flows from Investing Activities

Net cash provided by investing activities for the nine months ended September 30, 2022 was $43.5 million and resulted primarily from the proceeds from maturity of marketable securities of $110.4 million. This was offset by the purchases of marketable securities of $66.2 million and property and equipment of $0.7 million.

Net cash used in investing activities for the nine months ended September 30, 2021 was $19.9 million and resulted primarily from the purchases of marketable securities of $98.0 million and property and equipment of $0.5 million. This was offset by proceeds from maturity of marketable securities of $77.3 million and proceeds from redemption of marketable securities of $1.3 million.

Cash Flows from Financing Activities

Net cash provided by financing activities for the nine months ended September 30, 2022 totaled $0.2 million, primarily related to ESPP contributions.

Net cash provided by financing activities for the nine months ended September 30, 2021 totaled $89.5 million, primarily related to net proceeds of $81.2 million from the sale of our common stock in underwritten public offerings in April and September 2021, $8.1 million from the sale of our common stock in the ATM offering program and proceeds of $0.4 million from exercise of stock options and ESPP contributions, offset by payments of withholding taxes for employees relating to restricted stock awards.

Funding Requirements

To date, we have not commercialized any products and have not achieved profitability. We anticipate that we will continue to incur substantial net losses for the next several years as we further develop our product candidates, invest in our proprietary platform technology and operate as a publicly traded company.

We are currently generating revenue from our Roche collaboration but have not generated any product revenue since our inception and do not expect to generate any product revenue unless we receive regulatory approval for our product candidates. We believe that our cash, cash equivalents, and short-term marketable securities as of September 30, 2022, will be sufficient to meet our anticipated cash requirements for at least the next 12 months from the date of this filing. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially and negatively as a result of a number of factors, including the factors discussed in the section entitled “Risk Factors” in this Quarterly Report on Form 10-Q. We have based our estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect.

Due to the numerous risks and uncertainties associated with the development of our product candidates, we are unable to estimate precisely the amounts of capital outlays and operating expenditures necessary to complete the development of, and to obtain regulatory approval for, our product candidates. Our funding requirements will depend on many factors, including, but not limited to, the following:

- the success of our research and development efforts;
- the initiation, progress, timing, costs and results of clinical trials for our product candidates;
- the time and costs involved in obtaining regulatory approvals for our product candidates;
- the progress, timing and costs involved in developing manufacturing processes and agreements with third-party manufacturers;
- the rate of progress and cost of our commercialization activities;
- the expenses we incur in marketing and selling our product candidates;
- the revenue generated by sales of our product candidates;

- the emergence of competing or complementary technological developments;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the terms and timing of any additional collaborative, licensing or other arrangements that we may establish;
- the acquisition of businesses, products and technologies;
- our need to implement additional infrastructure and internal systems;
- our need to add personnel and financial and management information systems to support our product development and potential future commercialization efforts, and to enable us to operate as a public company; and
- the extent to which our business is adversely impacted by the effects of the coronavirus outbreak or by other health epidemics or pandemics; and
- other risks and uncertainties, including those listed under Part II, Item IA. "Risk Factors".

As an early-stage company, we are subject to a number of risks common to other life science companies, including, but not limited to, the ability to raise additional capital, development by our competitors of new technological innovations, risk of failure in preclinical studies, the safety and efficacy of our product candidates in clinical trials, the regulatory approval process, the ability to efficiently manufacture our products, market acceptance of our products once approved, lack of marketing and sales history, dependence on key personnel and protection of proprietary technology. Our therapeutic programs are currently pre-commercial, spanning discovery through early development and will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization of any product candidates. These efforts require significant amounts of additional capital, adequate personnel infrastructure and extensive compliance-reporting capabilities. There can be no assurance that our research and development will be successfully completed, that adequate protection for our intellectual property will be obtained, that any products developed will obtain necessary regulatory approval or that any approved products will be commercially viable. Even if our product development efforts are successful, it is uncertain when, if ever, we will generate revenue from product sales. We may never achieve profitability, and unless and until we do, we will continue to need to raise additional capital or obtain financing from other sources, such as strategic collaborations or partnerships. If we cannot expand our operations or otherwise capitalize on our business opportunities because we lack sufficient capital, our business, financial condition and results of operations could be materially adversely affected.

Contractual Commitments and Obligations

There have been no material changes to our contractual obligations and commitments set forth under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations- Contractual Obligations and Commitments" in our 2021 Annual Report.

Related Party Transactions

For a description of transactions with related parties which may fall outside of the reporting period of this section, please see the section entitled "*Certain Relationships and Related Person Transactions"* in our proxy statement filed with the SEC on April 27, 2022.

Recently Issued Accounting Pronouncements

For detailed information regarding recently issued accounting pronouncements and the expected impact on our consolidated financial statements, see Note 2, *Summary of Significant Accounting Policies* in the notes to the unaudited consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide this information required under this item.

Item 4. Controls and Procedures

Definition and limitations of disclosure controls

Our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the Exchange Act)) are controls and other procedures that are designed to ensure that information required to be disclosed in our reports filed under the Exchange Act, such as this report, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures are also designed to ensure that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Our management evaluates these controls and procedures on an ongoing basis.

There are inherent limitations to the effectiveness of any system of disclosure controls and procedures. These limitations include the possibility of human error, the circumvention or overriding of the controls and procedures and reasonable resource constraints. In addition, because we have designed our system of controls based on certain assumptions, which we believe are reasonable, about the likelihood of future events, our system of controls may not achieve its desired purpose under all possible future conditions. Accordingly, our disclosure controls and procedures provide reasonable assurance, but not absolute assurance, of achieving their objectives.

Evaluation of Disclosure Controls and Procedures

Our principal executive officer and principal financial officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) as of the end of the period covered by this Form 10-Q, have concluded that, based on such evaluation, our disclosure controls and procedures were effective to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms, and is accumulated and communicated to our management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

Changes in Internal Control

There have not been any changes in our internal controls over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) identified in connection with the evaluation of such internal control that occurred during our fiscal quarter ended September 30, 2022 that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

PART II – OTHER INFORMATION

Item 1. Legal Proceedings.

We are not currently a party to any material legal proceedings.

1A. Risk Factors.

Investing in our common stock involves a high degree of risk. Our business, prospects, financial condition or operating results could be materially adversely affected by the risks identified below, as well as other risks not currently known to us or that we currently consider immaterial. Furthermore, these factors represent risks and uncertainties that could cause actual results to differ materially from those implied by forward-looking statements. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risk factors, in its entirety, in addition to other information contained in this Quarterly Report on Form 10-Q and our other public filings with the SEC. The following risk factors may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future.

In the following discussion of risk factors, References to "we", "us", "our" and similar terms refer to the combined business of Synlogic, Inc. after the Merger on August 28, 2017.

Summary of Risk Factors

Our business is subject to numerous risks and uncertainties, including those highlighted in this section below, that represent challenges that we face in connection with the successful implementation of our strategy. The occurrence of one or more of the events or circumstances described in more detail in the risk factors below, alone or in combination with other events or circumstances, may have an adverse effect on our business, cash flows, financial condition and results of operations. Such risks include, but are not limited to:

- We are a clinical-stage biopharmaceutical company with a history of losses, and we expect to continue to incur losses for the foreseeable future, and we may never achieve or maintain profitability.
- We will require substantial additional funding, which may not be available on acceptable terms, or at all.
- Our quarterly and annual operating results may fluctuate in the future. As a result, we may fail to meet the expectations of research analysts or investors, which could cause our stock price to decline.
- Our stock price is volatile, and our stockholders may not be able to resell shares of our common stock at or above the price they paid.
- Our short operating history may make it difficult for stockholders to evaluate the success of our business to date and to assess our future viability.
- Clinical trials are costly, time consuming and inherently risky, and we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.
- The approach we are taking to discover and develop novel therapeutics using synthetic biology to create novel medicines is unproven and may never lead to marketable products.
- Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial viability of an approved label, or result in significant negative consequences following marketing approval, if any.
- Product development involves a lengthy and expensive process with an uncertain outcome, and results of earlier preclinical studies and clinical trials may not be predictive of future clinical trial results.
- If we experience delays or difficulties in the enrollment of patients in clinical trials, our costs might be higher than expected and our receipt of necessary regulatory approvals could be delayed or prevented.
- We may face potential product liability claims, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use or misuse of our product candidates harms patients or is perceived to harm patients even when such harm is unrelated to our product candidates, our regulatory approvals, if any, could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims. If we are unable to obtain adequate insurance or are required to pay for liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage, such liability could adversely affect our financial condition.

- A pandemic, epidemic, or outbreak of an infectious disease, such as COVID-19, or geopolitical tensions, such as the armed conflict between Russia and Ukraine, may materially and adversely affect our business and our financial results.
- Even if we obtain regulatory approval for a product candidate, we will remain subject to ongoing regulatory requirements.
- We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.
- We may be subject to, or may in the future become subject to, U.S. federal and state, and foreign laws and regulations imposing obligations on how we collect, use, disclose, store and process personal information. Our actual or perceived failure to comply with such obligations could result in liability or reputational harm and could harm our business. Ensuring compliance with such laws could also impair our efforts to maintain and expand our customer base, and thereby decrease our revenue.
- If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business, financial condition or results of operations.
- Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.
- Ethical, legal and social concerns about synthetic biology and genetic engineering could limit or prevent the use of our technologies and limit our revenues.
- We may not be successful in obtaining or maintaining necessary rights to Synthetic Biotics, product candidates and processes for our development pipeline through acquisitions and in-licenses.
- We may not have sufficient patent term protections for our product candidates to effectively protect our business.
- If we are unable to maintain effective proprietary rights for our product candidates or any future product candidates, we may not be able to compete effectively in our proposed markets.
- Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.
- We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful.
- We may be subject to claims challenging the inventorship of our patents and other intellectual property.
- We may not be able to protect our intellectual property rights throughout the world.
- We rely, and expect to continue to rely, on third parties to conduct some aspects of our product formulation, research, preclinical, and clinical studies, and those third parties may not perform satisfactorily, including by failing to meet deadlines for the completion of such formulation, research or testing.
- We rely on third-party supply and manufacturing partners for drug supplies for our late-stage clinical activities and may do the same for any commercial supplies of our product candidates.
- We may attempt to form collaborations in the future with respect to our product candidates, but we may not be able to do so, which may cause us to alter our development and commercialization plans.
- If the market opportunities for our product candidates are smaller than we believe they are, we may not meet our revenue expectations and, assuming approval of a product candidate, our business may suffer. Because the patient populations in the market for our product candidates may be small, we must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth.
- We face substantial competition, and our competitors may discover, develop or commercialize products faster or more successfully than us.
- Our employees, independent contractors, principal investigators, CROs, consultants and collaborators may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.
- Our employment agreements with our executive officers may require us to pay severance benefits to any of those persons who are terminated in connection with a change of control, which could harm our business, financial condition or results of operations.

- Our principal stockholders and management own a significant percentage of our stock and are able to exert significant control over matters subject to stockholder approval.
- Future sales of our common stock or securities convertible or exchangeable for our common stock may depress our stock price.
- Provisions of our charter documents or Delaware law could delay or prevent an acquisition of us, even if the acquisition would be beneficial to our stockholders and could make it more difficult for you to change management.
- We do not anticipate paying any cash dividends on our common stock in the foreseeable future; therefore, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Risks Related to Our Financial Condition, Capital Requirements and Operating Results

We are a clinical-stage biopharmaceutical company with a history of losses, and we expect to continue to incur losses for the foreseeable future, and we may never achieve or maintain profitability.

We are a clinical-stage biopharmaceutical company focused on the development of Synthetic Biotics and we have incurred significant operating losses since our inception. Our net loss was approximately $17.9 million and $49.5 million for the three and nine months ended September 30, 2022, respectively and $16.0 million and $45.5 million for the three and nine months ended September 30, 2021, respectively. As of September 30, 2022, we had an accumulated deficit of approximately $340.3 million. To date, we have not generated any product revenue. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We have no products on the market and expect that it will be many years, if ever, before we have a product candidate approved for commercialization.

We have not generated, and do not expect to generate, any product revenue for the foreseeable future, and we expect to continue to incur significant operating losses for the foreseeable future due to the cost of research and development, preclinical studies and clinical trials, the regulatory review process for product candidates, and the development of manufacturing and marketing capabilities for any product candidates approved for commercial sale. The amount of our potential future losses is uncertain. To achieve profitability, we must successfully develop product candidates, obtain regulatory approvals to market and commercialize product candidates, manufacture any approved product candidates on commercially reasonable terms, establish a sales and marketing organization or suitable third-party alternatives for any approved product candidates and raise sufficient funds to finance our business activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease our value and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in our value could also cause our stockholders to lose all or part of their investment.

We will require substantial additional funding, which may not be available on acceptable terms, or at all.

We have used substantial funds to discover and develop our programs and proprietary drug development platform in synthetic biology and will require substantial additional funds to conduct further research and development, including preclinical studies and clinical trials of our product candidates, seek regulatory approvals for our product candidates and manufacture and market any products that are approved for commercial sale. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect. Our monthly spending levels vary based on new and ongoing research and development and corporate activities. Because we cannot be certain of the length of time or activities associated with successful development and commercialization of our product candidates, we are unable to estimate the actual funds we will require to develop and commercialize them.

We do not expect to realize any appreciable revenue from product sales or royalties in the foreseeable future, if at all. Our revenue sources will remain very limited unless and until our product candidates complete clinical development and are approved for commercialization and successfully marketed or we enter into third-party arrangements with collaborators. To date, we have primarily financed our operations through sales of our securities, our third-party collaborations and the Merger. We intend to seek additional funding in the future through collaborations, equity or debt financings, credit or loan facilities or a combination of one or more of these financing sources. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms or at all. If we raise additional funds by issuing equity or convertible debt securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, may involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of equity securities received any distribution of corporate assets.

If we are unable to obtain funding on a timely basis or on acceptable terms, or at all, we may have to delay, limit or terminate our research and development programs and preclinical studies or clinical trials, if any, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our product candidates or technologies that we would otherwise pursue on our own.

Our quarterly and annual operating results may fluctuate in the future. As a result, we may fail to meet the expectations of research analysts or investors, which could cause our stock price to decline.

Our financial condition and operating results may fluctuate from quarter to quarter and year to year in the future due to a variety of factors, many of which are beyond our control. Factors relating to our business that may contribute to these fluctuations include the following factors, as well as factors described elsewhere in this Quarterly Report on Form 10-Q and others:

- our ability to achieve or maintain profitability;
- our ability to develop and maintain Synthetic Biotic technologies;
- our ability to manage our growth;
- the outcomes of research programs, clinical trials, or other product development and approval processes;
- our ability to accurately report our financial results in a timely manner;
- our dependence on, and the need to attract and retain, key management and other personnel;
- our ability to obtain, protect and enforce our intellectual property rights;
- our ability to prevent the theft or misappropriation of our intellectual property, know-how or technologies;
- our ability to achieve milestones with our collaborators, such as Roche;
- potential advantages that our competitors and potential competitors may have in securing funding or developing competing technologies or products; and
- our ability to obtain additional capital that may be necessary to expand our business.

Due to the various factors mentioned above, and others, the results of any prior quarterly or annual periods should not be relied upon as indications of our future operating performance.

Our stock price is volatile, and our stockholders may not be able to resell shares of our common stock at or above the price they paid.

The trading price of our common stock is highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, such as reports by industry analysts, investor perceptions, general industry trends or negative announcements by other companies involving similar technologies or diseases. These factors also include those discussed in this “Risk Factors” section of this Quarterly Report on Form 10-Q and others such as:

- announcements relating to collaborations that we may enter into with respect to the development or commercialization of our product candidates;
- announcements relating to the receipt, modification or termination of government contracts or grants;
- termination or delay of a development program;
- product liability claims related to our clinical trials or product candidates;
- prevailing economic conditions;
- perspectives on synthetic biology and genetic engineering;
- additions or departures of key personnel;
- business disruptions caused by natural disasters;
- disputes concerning our intellectual property or other proprietary rights;
- FDA or other U.S. or foreign regulatory actions affecting us or our industry;

- sales of our common stock by the company, our executive officers and directors or our stockholders in the future;
- future sales or issuances of equity or debt securities by us;
- lack of an active, liquid and orderly market in our common stock;
- fluctuations in our quarterly operating results; and
- the issuance of new or changed securities analysts' reports or recommendations regarding us.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that have been often unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business.

Our short operating history may make it difficult for stockholders to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage biopharmaceutical company with a limited operating history. We commenced active operations in 2014. Our operations to date have been limited to organizing and staffing our company, research and development activities, business planning and raising capital. We will need to transition from a company with a focus on research and clinical development to a company capable of commercial activities. We have not yet demonstrated our ability to successfully complete large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale product, or arrange for a third-party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Typically, it takes many years to develop one new product candidate from the time it is discovered to the time that it becomes available for treating patients. We may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors that may hinder our success in commercializing one or more of our product candidates. Further, drug development is a capital-intensive and highly speculative undertaking that involves a substantial degree of risk. You should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early stages of development and clinical trials. Any forward-looking statements regarding our future prospects, plans or viability may not be as accurate as they may be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

Risks Related to the Development of Our Product Candidates

Clinical trials are costly, time consuming and inherently risky, and we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Clinical development of a product candidate is expensive, time consuming and involves significant risk. We cannot guarantee that any clinical trials we undertake to conduct will be conducted as planned or completed on schedule or at all. A failure of one or more clinical trials can occur at any stage of development. Events that may prevent successful or timely completion of clinical development of our product candidates include but are not limited to:

- inability to generate satisfactory preclinical or other nonclinical data, including, toxicology, or other *in vivo* or *in vitro* data or diagnostics to support the initiation or continuation of clinical trials;
- delays in reaching agreement on acceptable terms with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in obtaining required institutional review board approval at each clinical trial site;
- failure to permit the conduct of a clinical trial by regulatory authorities, after review of an investigational new drug or equivalent foreign application or amendment;
- delays in recruiting qualified patients in our clinical trials;
- failure by clinical sites or CROs or other third parties to adhere to clinical trial requirements;

- failure by us, clinical sites, CROs or other third parties to perform in accordance with the good clinical practices requirements of the FDA or applicable foreign regulatory guidelines;
- patients dropping out of the clinical trials;
- occurrence of adverse events, unacceptable side effects or toxicity issues associated with our product candidates;
- imposition by the FDA of a clinical hold or the requirement by other similar regulatory agencies that one or more clinical trials be delayed or halted;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols or performing additional nonclinical studies;
- the ultimate affordability of the cost of clinical trials of our product candidates;
- negative or inconclusive results from our clinical trials that may result in us deciding, or regulators requiring us, to conduct additional clinical trials or abandon such clinical trials and/or clinical trials or development programs in other ongoing or planned indications for a product candidate; and
- delays in identifying or reaching agreement on acceptable terms with third-party manufacturers, delays in developing and transferring a reproducible, scalable manufacturing process, or delays or failure in manufacturing sufficient quantities of our product candidates for use in clinical trials.

Any inability to successfully complete clinical development and obtain regulatory approval for our product candidates could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional preclinical studies and/or clinical trials, or the results obtained from such new formulation may not be consistent with previous results obtained. Clinical trial delays could also shorten any anticipated periods of patent exclusivity for our product candidates and may allow competitors to develop and bring products to market before we do which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

The approach we are taking to discover and develop novel therapeutics using synthetic biology to create novel medicines is unproven and may never lead to marketable products.

The scientific discoveries that form the basis for our efforts to generate and develop our product candidates are relatively recent. The scientific evidence to support the feasibility of developing drugs based on our approach is both preliminary and limited. Synthetic Biotics represent a novel therapeutic modality and their successful development by us may require additional studies and efforts to optimize their therapeutic potential. Any product candidates that we develop may not demonstrate in patients the therapeutic properties ascribed to them in laboratory and other preclinical studies, and they may interact with human biological systems in unforeseen, ineffective or even harmful ways. We have also not yet succeeded and may never succeed in demonstrating efficacy and safety for our current or any future product candidates in a pivotal clinical trial. If we are not able to successfully develop and commercialize product candidates based upon this technological approach, we may never become profitable, and the value of our capital stock may decline.

Our Synthetic Biotic product candidates are based on a relatively novel technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval, if at all.

We have concentrated our research and development efforts to date on a limited number of product candidates based on our Synthetic Biotic therapeutic platform, including demonstrating proof of concept of our lead program in PKU, proof of mechanism for enteric hyperoxaluria, and the initiation of IND-enabling for a potential treatment for HCU. Our future success depends on our successful development of viable product candidates. There can be no assurance that we will not experience problems or delays in developing our product candidates and that such problems or delays will not cause unanticipated costs, or that any such development problems can be solved.

The clinical trial and manufacturing requirements of the FDA, the EMA and other regulatory authorities, and the criteria these regulators use to determine the safety and efficacy of a product candidate, vary substantially according to the type, complexity, novelty and intended use and market of the product candidate. The regulatory approval process for novel product candidates such as Synthetic Biotics may be more expensive and take longer than for other, better known or more extensively studied therapeutic modalities. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or the European Union or how long it will take to commercialize our product candidates, even if approved for marketing. Approvals by the EMA or national regulatory agencies may not be indicative of what the FDA, and vice versa, may require for approval and different or additional preclinical studies or clinical trials may be required to support regulatory approval in each respective jurisdiction. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product candidate to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects may be harmed.

We may not be successful in our efforts to use and expand our development platform to build a pipeline of product candidates.

A key element of our strategy is to use our targeted focus and experienced management and scientific team to create Synthetic Biotics that can be deployed against a broad range of human diseases in order to build a pipeline of product candidates. Although our research and development efforts to date have resulted in potential product candidates, we may not be able to continue to identify and develop additional product candidates. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development. For example, these potential product candidates may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our approach, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position. There is no assurance that we will be successful in our preclinical and clinical development, and the process of obtaining regulatory approvals will, in any event, require the expenditure of substantial time and financial resources.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial viability of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or terminate our clinical trials or result in a restrictive label or delay regulatory approval by the FDA or comparable foreign authorities. Undesirable side effects and negative results for other indications may negatively impact the development and potential for approval of our product candidates for their proposed indications.

Additionally, even if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of or revoke licenses for such products;
- regulatory authorities may require additional warnings on the labels of such products;
- we may be required to create a REMS plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, and/or other elements to assure safe use;
- we may be required to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety of the product;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of a product candidate, even if approved, and could significantly harm our business, results of operations, and prospects.

Our product development program may not uncover all possible adverse events that patients who take our product candidates may experience. The number of subjects exposed to our product candidates during clinical trials and the average exposure time in the clinical development program may be inadequate to detect rare adverse events, or chance findings, that may only be detected once the product is administered to more patients and for greater periods of time.

Clinical trials by their nature use a sample of the potential patient population. However, with a limited number of patients and limited duration of exposure, we cannot be fully assured that uncommon or severe side effects of our product candidates will be uncovered. Such side effects may only be uncovered with a significantly larger number of patients exposed to the drug. If such safety problems occur or are identified after a product candidate reaches the market, the FDA may require that we amend the labeling of the product or recall the product or may even withdraw approval for the product. Any of these events could prevent us from achieving or maintaining market acceptance of a product candidate, even if approved, and could significantly harm our business, results of operations, and prospects.

We are heavily dependent on the success of our product candidates. Some of our product candidates have produced results in preclinical and clinical settings to date, but none of our product candidates has completed all required clinical trials, and we cannot give any assurance that we will generate data for any of our product candidates sufficient to receive regulatory approval in our planned indications, which will be required before they can be commercialized.

We have invested substantially all of our efforts and financial resources to identify, acquire and develop our portfolio of product candidates. Our future success is dependent on our ability to successfully further develop, obtain regulatory approval for, and commercialize one or more product candidates. We currently generate no revenue from sales of any products, and we may never be able to develop or commercialize a product candidate.

On August 20, 2019, we announced that we were discontinuing our first therapeutic program to enter clinical trials, SYNB1020, an early-stage clinical product candidate for the treatment of hyperammonemia. The decision to discontinue the program was based on top-line data from an interim analysis of a randomized, double-blind, placebo-controlled Phase 1b/2a clinical trial of the Synthetic Biotic medicine in 23 patients with cirrhosis and elevated blood ammonia. While SYNB1020 was well-tolerated in Phase 1b/2a clinical trial, the trial showed it did not lower blood ammonia in patients with cirrhosis. As a result, we have become more dependent on the success of our SYNB1934, SYNB8802 and SYNB1353 programs.

In addition, none of our product candidates has advanced into any pivotal clinical trial for our proposed indications and it may be years before any pivotal clinical trials are initiated and completed, if at all. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. We cannot be certain that any of our product candidates will be successful in clinical trials or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

If we fail to obtain or maintain orphan drug exclusivity for some of our products, our competitors may obtain approval to sell competing drugs to treat the same conditions and our revenues will be reduced.

As part of our business strategy, we have developed and may in the future develop product candidates that may be eligible for FDA and European Commission orphan drug designation. In October 2017, the FDA granted orphan drug designation to SYNB1618 for the treatment of PKU. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat, diagnose or prevent rare diseases or conditions that affect fewer than 200,000 people in the United States. In the EU, orphan drug designation may be granted to drugs intended to treat, diagnose or prevent a life-threatening or chronically debilitating disease having a prevalence of no more than five in 10,000 people in the EU. In May 2022, the EMA granted orphan designation to SYNB1618 for the treatment of PKU. The company that first obtains FDA approval for a designated orphan drug for the associated rare disease receives marketing exclusivity for use of that drug for the stated condition for a period of seven years. Orphan drug exclusive marketing rights may be lost under several circumstances, including a later determination by the FDA that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug. Similar regulations are in effect in the EU with a ten-year period of market exclusivity.

Because the extent and scope of patent protection for some of our product candidates may be limited, obtaining orphan drug designation is especially important for any product candidates that may be eligible for orphan drug designation. For eligible products, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug designation for our product candidates that do not have broad patent protection, our competitors may then seek to sell a competing drug to treat the same condition and our revenues, if any, may be adversely affected thereby.

Even though we have obtained orphan drug designation for one of our product candidates and intend to seek orphan drug designation for other product candidates, there is no assurance that we will be the first to obtain marketing approval for any particular rare indication. Further, even though we have obtained orphan drug designation for certain of our product candidates, or even if we obtain orphan drug designation for other potential product candidates, such designation may not effectively protect us from competition because different drugs can be approved for the same condition and the same drug can be approved for different conditions and potentially used off-label in the orphan indication. Even after an orphan drug is approved, the FDA can subsequently approve a competing drug for the same condition for several reasons, including, if the FDA concludes that the later drug is safer or more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process.

Product development involves a lengthy and expensive process with an uncertain outcome, and results of earlier preclinical studies and clinical trials may not be predictive of future clinical trial results.

The results from preclinical studies or early clinical trials of a product candidate may not predict the results that will be obtained in subsequent subjects or in later stage clinical trials of that product candidate or any other product candidate. Flaws in the design of a

clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and we may be unable to design and execute clinical trials to support regulatory approval of our product candidates. In addition, preclinical study and clinical trial data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain regulatory authority approval. Product candidates that seemingly perform satisfactorily in preclinical studies and clinical trials may nonetheless fail to obtain regulatory approval. There is a high failure rate for drugs proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway, or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Any such setbacks in our clinical development could negatively affect our business and operating results.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our costs might be higher than expected and our receipt of necessary regulatory approvals could be delayed or prevented.

Clinical trials of a new product candidate require the enrollment of a sufficient number of healthy volunteers or patients suffering from the disease or condition the product candidate is intended to treat and who meet other eligibility criteria. The timing of our clinical trials depends on our ability to recruit eligible subjects to participate as well as the completion of required follow-up evaluations. Patients and healthy volunteers may be unwilling to participate in our clinical trials because of negative publicity from adverse events related to novel therapeutic approaches, competitive clinical trials for similar patient populations, the existence of current treatments or for other reasons including due to concerns posed by the COVID-19 pandemic. Rates of patient enrollment are affected by many factors, including the size of the potential patient population, the age and condition of the patients, the stage and severity of disease or condition, the nature and requirements of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease or condition, the perceived risks, the clinical trial administration practices of the CRO or clinical trial sites, labor shortages at the CRO or clinical trial sites, benefits and convenience of administration of the product candidate being studied, the patient referral practices of physicians, the amount of attention provided to our trial by clinical trial sites, our efforts and CRO efforts to facilitate timely enrollment in clinical trials, and the eligibility criteria for the clinical trial. Delays or difficulties in patient enrollment or difficulties retaining trial participants, including as a result of the availability of existing or other investigational treatments, can result in increased costs, longer development times or termination of a clinical trial.

In addition, our success may depend, in part, on our ability to identify patients who qualify for our clinical trials or are likely to benefit from any product candidate that we may develop, which will require those potential patients to undergo a screening assay for the presence or absence of a particular genetic sequence or clinical trait. Genetically defined diseases generally, and especially those for which our current product candidates are targeted, may have relatively low prevalence. For example, we estimate there are approximately 17,000 patients that may be diagnosed with PKU in the United States. If we, or any third parties that we engage to assist us, are unable to successfully identify patients with these diseases, or experience delays in doing so, then we may not realize the full commercial potential of any product candidate we develop.

We may face potential product liability claims, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use or misuse of our product candidates harms patients or is perceived to harm patients even when such harm is unrelated to our product candidates, our regulatory approvals, if any, could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims. If we are unable to obtain adequate insurance or are required to pay for liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage, such liability could adversely affect our financial condition.

The use or misuse of our product candidates in clinical trials and the sale of any products for which we may obtain marketing approval exposes us to the risk of potential product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our product candidates and approved products, if any. There is a risk that our product candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. Patients with the diseases targeted by our product candidates may already be in severe and advanced stages of disease and have both known and unknown significant pre-existing and potentially life-threatening health risks. During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our products, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which an adverse event is unrelated to our product candidates, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may delay our regulatory approval process or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

Although we have product liability insurance, which covers any clinical trial we may conduct in the United States, our insurance may be insufficient to reimburse us for any expenses or losses we may suffer. We will also likely be required to increase our product liability insurance coverage for the advanced clinical trials that we plan to initiate. If we obtain marketing approval for any of our product candidates, we will need to expand our insurance coverage to include the sale of commercial products. There is no way to know if we will be able to continue to obtain product liability coverage and obtain expanded coverage we may require, in sufficient amounts to protect us against losses due to liability, on acceptable terms, or at all. We may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage. Where we have provided indemnities in favor of third parties under our agreements with them, there is also a risk that these third parties could incur liability and bring a claim under such indemnities. An individual may bring a product liability claim against us alleging that one of our product candidates or products causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. Any product liability claim brought against us, with or without merit, could result in:

- withdrawal of clinical trial volunteers, investigators, patients or trial sites or limitations on approved indications;
- the inability to commercialize, or if commercialized, decreased demand for, our product candidates;
- if commercialized, product recalls, withdrawals of labeling, marketing or promotional restrictions or the need for product modification;
- initiation of investigations by regulators;
- loss of revenues;
- substantial costs of litigation, including monetary awards to patients or other claimants;
- liabilities that substantially exceed our product liability insurance, which we would then be required to pay ourselves;
- an increase in our product liability insurance rates or the inability to maintain insurance coverage in the future on acceptable terms, if at all;
- the diversion of management's attention from our business;
- loss of key employees; and
- damage to our reputation and the reputation of our products and our technology.

Product liability claims may subject us to the foregoing and other risks, which could have a material adverse effect on our business, financial condition or results of operations.

We or the third parties upon which we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

A pandemic, epidemic, or outbreak of an infectious disease, such as COVID-19, or geopolitical tensions, such as the armed conflict between Russia and Ukraine, may materially and adversely affect our business and our financial results.

The coronavirus outbreak and the armed conflict between Russia and Ukraine has affected segments of the global economy and may materially affect our operations, including potentially significant interruption of our clinical trial activities. The continued spread of the coronavirus may result in a period of business disruption, including material delays in our clinical trials. In addition, there could be a potential effect of COVID-19 to the business at the FDA or other health authorities, which could result in delays of reviews and approvals, including with respect to our product candidates. For example, in 2021, we experienced delays with the FDA that we believe were related to COVID-19. In addition, clinical site initiation and patient enrollment may be delayed due to prioritization of healthcare system resources toward the COVID-19 pandemic. For example, in 2021, the ability of site IRBs to meet and review protocol amendments were delayed due to COVID-19. Sites were also unable at times to schedule in-person screening visits with potential patients during certain times in 2021. Our CROs and clinical trial sites also experienced labor shortages in 2021 and 2020. Some patients may not be able to comply with clinical trial protocols if quarantines or their concerns about COVID-19 impede patient movement or interrupt healthcare services. Similarly, the ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 has adversely impacted our clinical trial operations.

The continued spread globally could also have a material adverse effect on our clinical trial operations in the United States and elsewhere, including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if an outbreak occurs in their geography.

We continue to monitor the potential impact of the coronavirus outbreak, and any associated restrictions on travel and work that have been implemented, on our business and pre-clinical and clinical trials. The extent to which the coronavirus impacts us will depend on future developments, which are uncertain and cannot be predicted, including new information which may emerge concerning the severity of the coronavirus and the actions to contain the coronavirus or treat its impact, among others. We will continue to carefully monitor the situation with respect to each of our clinical trials and follow guidance from local and federal health authorities.

COVID-19 may also affect employees of third-party contract research organizations and contract manufacturing organizations located in affected geographies that we rely upon to carry out our clinical trials. For example, there were delays in laboratory analyses of patient samples due to pandemic related staffing issues at our contract research organizations. In addition, we have taken precautionary measures, for example, mandating vaccines, and may take additional measures, intended to help minimize the risk of the virus to our employees. We will continue to adjust these measures as necessary and as we are able in the future to balance the needs of the business with the safety of our employees.

We cannot presently predict the extent to which current or future business shutdowns and disruptions may impact or limit our ability or the ability of any of the third parties with which we engage to conduct business in the manner and on the timelines presently planned. Any such impacts or limitations could have a material adverse impact on our business and our results of operation and financial condition. While the potential economic impact brought by and the duration of the coronavirus outbreak may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, potentially reducing our ability to access capital, which could in the future negatively affect our liquidity. Similarly, the current conflict between Ukraine and Russia has created extreme volatility in the global capital markets and is expected to have further global economic consequences, including disruptions of the global supply chain and energy markets. A recession or market correction resulting from the spread of COVID-19 or the geopolitical tensions in Russia and Ukraine, could materially affect our business and the price of our common stock.

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

The regulatory approval processes of the FDA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain marketing approval for a novel therapeutic product from the FDA and other comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, laws or regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for commercialization, of any product candidate and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain that approval.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or other comparable foreign regulatory authorities that our product candidates are safe, pure and potent or effective for their proposed indications;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or other comparable foreign regulatory authorities in order to support approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a BLA, to the FDA or other equivalent marketing authorization application submissions to obtain regulatory approval in the United States or elsewhere;

- upon review of our clinical trial sites and data, the FDA or comparable foreign regulatory authorities may find our record keeping or the record keeping of our clinical trial sites or investigators to be inadequate;
- the FDA or other comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or other comparable foreign regulatory authorities or the laws they enforce may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, financial condition and results of operations. The FDA and other comparable foreign regulatory authorities have substantial discretion in the approval process and determining when or whether to grant regulatory approval will be obtained for any of our product candidates, and whether to impose any conditions on such marketing approvals as described below. Even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA or other comparable foreign regulatory authorities.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, if any, they may grant approval contingent on the performance of costly post-marketing clinical trials, or they may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate or with restrictive risk mitigation measures or warning language or contraindications that make the approved product more difficult or costly to commercialize. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

We may seek breakthrough therapy designation for one or more of our product candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek a breakthrough therapy designation from the FDA for some of our product candidates. A breakthrough therapy is defined as a drug or biological product that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and for which preliminary clinical evidence indicates that the drug or biological product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs or biological products that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development. Drugs designated as breakthrough therapies by the FDA could also be eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to grant such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify and are designated as breakthrough therapies, the FDA may later decide that the drugs or biological products no longer meet the conditions for designation and the designation may be rescinded.

We have received Fast Track designation for one of our product candidates and may seek such designation for one or more of our other product candidates, but we might not receive such designation, and even if we do, such designation may not actually lead to a faster development or regulatory review or approval process.

If a product candidate is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for the condition, a product sponsor may apply for Fast Track designation. We were awarded Fast Track designation for SYNB1618 in April 2018 and for SYNB1353 in August 2022. Fast Track designation does not ensure that we will receive marketing approval for the product candidate or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with Fast Track designation compared to conventional FDA procedures. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast Track designation alone does not guarantee qualification for the FDA's priority review procedures.

Even if we obtain regulatory approval for a product candidate, we will remain subject to ongoing regulatory requirements.

If any of our product candidates are approved for marketing, we will be subject to ongoing regulatory requirements, including with respect to manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing clinical trials, and submission of safety, efficacy and other post-approval information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to continuously comply with FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to current good manufacturing practices (cGMP) regulations and corresponding foreign regulatory manufacturing requirements. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any BLA or marketing authorization application.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product candidate may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. We will be required to report adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. If our original marketing approval for a product candidate was obtained through an accelerated approval pathway, we could be required to conduct a successful post-marketing clinical trial in order to confirm the clinical benefit for our products. An unsuccessful post-marketing clinical trial or failure to complete such a trial could result in the withdrawal of marketing approval.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, the regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue untitled or warning letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval or revoke a license;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- require a product recall.

Any government investigation of alleged violations of law would be expected to require us to expend significant time and resources in response and could generate adverse publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to develop and commercialize our products and our value and operating results would be adversely affected.

Obtaining and maintaining marketing approval of our current and future product candidates in one jurisdiction does not mean that we will be successful in obtaining marketing approval of our current and future therapeutic product candidates in other jurisdictions.

Obtaining and maintaining marketing approval of our current and future product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain marketing approval in any other jurisdiction, while a failure or delay in obtaining marketing approval in one jurisdiction may have a negative effect on the marketing approval process in others. For example, even if the FDA grants marketing approval of a product candidate, comparable foreign regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our future products will also be subject to approval.

We may submit marketing applications in other countries in addition to the United States. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign marketing approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. The coronavirus pandemic has also adversely affected the operations of necessary government agencies. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Healthcare legislative reform measures may have a material adverse effect on our business, financial condition or results of operations.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "ACA"), was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The ACA, among other things, subjected biological products to potential competition by lower-cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs and biologics that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs and biologics, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (increased from 50% pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs and biologics to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs or biologics to be covered under Medicare Part D.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and as a result, certain sections of the ACA have not been fully implemented or have been effectively repealed through Executive Orders and/or executive agency actions. However, following several years of litigation in the federal courts, in June 2021, the U.S. Supreme Court upheld the ACA when it dismissed a legal challenge to the ACA's constitutionality. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, re-examining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

Further legislative and regulatory changes under the ACA remain possible, although the new federal administration under President Biden has signaled that it plans to build on the ACA and expand the number of people who are eligible for health insurance subsidies under it. It is unknown what form any such changes or any law would take, and how or whether it may affect the biopharmaceutical industry as a whole or our business in the future. We expect that changes or additions to the ACA, the Medicare and Medicaid programs, such as changes allowing the federal government to directly negotiate drug prices, and changes stemming

from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the health care industry in the US.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, resulted in reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through June 30, 2022 (a 1% sequester will apply from April 1, 2022 through June 30, 2022) due to the COVID-19 pandemic, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. As another example, the 2021 Consolidated Appropriations Act signed into law on December 27, 2020, incorporated extensive healthcare provisions and amendments to existing laws, including a requirement that all manufacturers of drugs and biological products covered under Medicare Part B report the product's average sales price, or ASP, to HHS beginning on January 1, 2022, subject to enforcement via civil money penalties.

In the United States and in some other jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the health care system that could prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities, or affect our ability to profitably sell any drug candidates for which we obtain marketing approval, if any. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, was intended to modernize the regulation of drugs and devices and to spur innovation, but its ultimate implementation is uncertain. Legislative proposals continue to be discussed in the U.S. Congress as potentially leading to a future "Cures 2.0" bill that is expected to have bipartisan support. In addition, in August 2017, the FDA Reauthorization Act was signed into law, which reauthorized the FDA's user fee programs and included additional drug and biological product provisions. The next legislative reauthorization must be completed in 2022, which has the potential to make further changes to FDA authorities or policies pertaining to biopharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals, if any, of our drug candidates, may be or whether such changes will have any other impacts on our business. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing conditions and other requirements.

Further, over the past several years there has been heightened governmental scrutiny over the manner in which biopharmaceutical manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. The probability of success of these newly announced policies, many of which have been subjected to legal challenge in the federal court system, and their potential impact on the U.S. prescription drug marketplace is unknown. There are likely to be continued political and legal challenges associated with implementing these reforms as they are currently envisioned, and the recent transition to a new Democrat-led presidential administration created further uncertainty in the health care and biopharmaceutical industries. For example, in July 2021, President Biden issued a sweeping executive order on promoting competition in the American economy that includes several mandates pertaining to the pharmaceutical and health care insurance industries. Among other things, the executive order directs the FDA to work towards implementing a system for importing drugs from Canada (following on a Trump administration notice-and-comment rulemaking on Canadian drug importation that was finalized in October 2020). The Biden order also called on HHS to release a comprehensive plan to combat high prescription drug prices, and it includes several directives regarding the Federal Trade Commission's oversight of potentially anticompetitive practices within the pharmaceutical industry. The drug pricing plan released by HHS in September 2021 in response to the executive order makes clear that the Biden Administration supports aggressive action to address rising drug prices, including allowing HHS to negotiate the cost of Medicare Part B and D drugs, but such significant changes will require either new legislation to be passed by Congress or time-consuming administrative actions. Accordingly, there remains a large amount of uncertainty regarding the federal government's approach to making pharmaceutical treatment costs more affordable for patients.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, California requires pharmaceutical manufacturers to notify certain purchasers, including health insurers and government health plans at least 60 days before any scheduled increase in the wholesale acquisition cost (WAC), of their product if the increase exceeds 16%, and further requires pharmaceutical manufacturers to explain whether a change or improvement in the product necessitates such an increase. Similarly, Vermont requires pharmaceutical manufacturers to disclose price information on certain prescription drugs, and to provide notification to the state if introducing a new drug with a WAC in excess of the Medicare Part D specialty drug threshold. In December 2020, the U.S. Supreme Court also held unanimously that federal

law does not preempt the states' ability to regulate pharmaceutical benefit managers, or PBMs, and other members of the healthcare and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts by states in this area. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates, if approved, or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or EU member state level may result in significant additional requirements or obstacles that may increase our operating costs.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action. We expect that additional federal and state health care reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for health care products and services, which could result in limited coverage and reimbursement and reduced demand for our products, once approved, or additional pricing pressures.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations. These laws may impact, among other things, our proposed sales, marketing, and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act, and its implementing regulations, which imposes specified requirements relating to the privacy, security, and transmission of individually identifiable health information;
- the federal physician payments sunshine requirements under the ACA require manufacturers of drugs, devices, biologics, and medical supplies to report annually to the HHS information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including governmental and private payors, to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and state laws governing the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform

legislation has strengthened these laws. For example, the ACA, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Moreover, the ACA provides that the U.S. government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We may be subject to, or may in the future become subject to, U.S. federal and state, and foreign laws and regulations imposing obligations on how we collect, use, disclose, store and process personal information. Our actual or perceived failure to comply with such obligations could result in liability or reputational harm and could harm our business. Ensuring compliance with such laws could also impair our efforts to maintain and expand our customer base, and thereby decrease our revenue.

In many activities, including the conduct of clinical trials, we are subject to laws and regulations governing data privacy and the protection of health-related and other personal information. These laws and regulations govern our processing of personal data, including the collection, access, use, analysis, modification, storage, transfer, security breach notification, destruction and disposal of personal data. We must comply with laws and regulations associated with the international transfer of personal data based on the location in which the personal data originates and the location in which it is processed. Although there are legal mechanisms to facilitate the transfer of personal data from the European Economic Area (EEA), and Switzerland to the United States, the decision of the European Court of Justice that invalidated the safe harbor framework has increased uncertainty around compliance with EU privacy law requirements. As a result of the decision, it was no longer possible to rely on safe harbor certification as a legal basis for the transfer of personal data from the European Union to entities in the United States. In February 2016, the European Commission announced an agreement with the Department of Commerce, or DOC, to replace the invalidated safe harbor framework with a new EU-U.S. "Privacy Shield." However, in July 2020, the Court of Justice of the EU (CJEU) limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU-US Privacy Shield for purposes of international transfers and imposing further restrictions on use of the standard contractual clauses (SCCs) including, a requirement for companies to carry out a transfer privacy impact assessment, which among other things, assesses laws governing access to personal data in the recipient country and considers whether supplementary measures that provide privacy protections additional to those provided under SCCs will need to be implemented to ensure an essentially equivalent level of data protection to that afforded in the EEA. The European Commission subsequently issued new SCCs in June 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board, and which are in turn relatively more onerous.

The privacy and security of personally identifiable information stored, maintained, received or transmitted, including electronically, is subject to significant regulation in the United States and abroad. While we strive to comply with all applicable privacy and security laws and regulations, legal standards for privacy continue to evolve and any failure or perceived failure to comply may result in proceedings or actions against us by government entities or others, or could cause reputational harm, which could have a material adverse effect on our business.

Numerous foreign, federal and state laws and regulations govern collection, dissemination, use and confidentiality of personally identifiable health information, including state privacy and confidentiality laws (including state laws requiring disclosure of breaches); federal and state consumer protection and employment laws; HIPAA; and European and other foreign data protection laws. These laws and regulations are increasing in complexity and number, may change frequently and sometimes conflict.

HIPAA establishes a set of national privacy and security standards for the protection of individually identifiable health information, including protected health information, or PHI, by health plans, certain healthcare clearinghouses and healthcare providers that submit certain covered transactions electronically, or covered entities, and their ''business associates,'' which are persons or entities that perform certain services for, or on behalf of, a covered entity that involve creating, receiving, maintaining or transmitting PHI. While we are not currently a covered entity or business associate under HIPAA, we may receive identifiable information from these entities. Failure to receive this information properly could subject us to HIPAA's criminal penalties, which may include fines up to $50,000 per violation and/or imprisonment. In addition, responding to government investigations regarding alleged violations of these and other laws and regulations, even if ultimately concluded with no findings of violations or no penalties imposed, can consume company resources and impact our business and, if public, harm our reputation.

In addition, various states, such as California and Massachusetts, have implemented similar privacy laws and regulations, such as the California Confidentiality of Medical Information Act, that impose restrictive requirements regulating the use and disclosure of health information and other personally identifiable information. In addition to fines and penalties imposed upon violators, some of these state laws also afford private rights of action to individuals who believe their personal information has been misused.

California's patient privacy laws, for example, provide for penalties of up to $250,000 and permit injured parties to sue for damages. In addition, California enacted the California Consumer Privacy Act (the CCPA), which took effect on January 1, 2020, became enforceable by the California Attorney General on July 1, 2020, and has been dubbed the first "GDPR-like" law in the United States. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used by requiring covered companies to provide new disclosures to California consumers (as that term is broadly defined) and provide such consumers new ways to opt-out of certain sales of personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the California Privacy Rights Act (the CPRA) recently passed in California. The CPRA will impose additional data protection obligations on companies doing business in California, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Although the CCPA currently exempts certain health-related information, including clinical trial data, the CCPA and the CPRA may increase our compliance costs and potential liability. Similar laws have been adopted in other states (for example Nevada, Virginia and Colorado) or proposed in other states and at the federal level, and if passed, such laws may have potentially conflicting requirements that would make compliance challenging.

The interplay of federal and state laws may be subject to varying interpretations by courts and government agencies, creating complex compliance issues for us and our clients and potentially exposing us to additional expense, adverse publicity and liability. Further, as regulatory focus on privacy issues continues to increase and laws and regulations concerning the protection of personal information expand and become more complex, these potential risks to our business could intensify.

In addition, the interpretation and application of consumer, health-related, and data protection laws are often uncertain, contradictory, and in flux.

The legislative and regulatory landscape for privacy and data security continues to evolve, and there has been an increasing focus on privacy and data security issues which may affect our business. Failure to comply with current and future laws and regulations could result in government enforcement actions (including the imposition of significant penalties), criminal and civil liability for us and our officers and directors, private litigation and/or adverse publicity that negatively affects our business.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business, financial condition or results of operations.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use, and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our research and development efforts, commercialization efforts and business operations and environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by us and our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of specified materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently, and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. Given the nature of the research and development work conducted by us, we do not currently carry biological or hazardous waste insurance coverage.

Laws and regulations governing international operations may preclude us from developing, manufacturing and selling certain products outside of the United States and require us to develop, implement and maintain costly compliance programs.

To develop, manufacture and sell certain products outside the United States, we must dedicate resources to comply with numerous laws and regulations in each jurisdiction in which we operate. The Foreign Corrupt Practices Act (FCPA), prohibits any United States individual or business from paying, offering, authorizing payment or offering anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and

fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees may be considered government employees or foreign officials. In other circumstances, certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-United States nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. These laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the U.S., which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions and export control laws.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. If any of the above events were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of preclinical or clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed, and the further development and commercialization of our product candidates could be delayed.

Ethical, legal and social concerns about synthetic biology and genetic engineering could limit or prevent the use of our technologies and limit our revenues.

Our technologies involve the use of synthetic biology and genetic engineering. Public perception about the safety and environmental hazards of, and ethical concerns over, synthetic biology and genetic engineering could influence public acceptance of our technologies, product candidates and processes. If we and our collaborators are not able to overcome the ethical, legal and social concerns relating to synthetic biology and genetic engineering, our technologies, product candidates and processes may not be accepted. These concerns could result in increased expenses, regulatory scrutiny and increased regulation, trade restrictions on imports of Synthetic Biotics, delays or other impediments to our programs or the public acceptance and commercialization of Synthetic Biotics. Further, there is a risk that Synthetic Biotics made using our technologies could result in adverse health effects or other adverse events, which could also lead to negative publicity. We design and produce product candidates with characteristics comparable or disadvantaged to those found in naturally occurring organisms or enzymes in a controlled laboratory; however, the release of such organisms into uncontrolled environments could have unintended consequences. Any adverse effect resulting from such a release could have a material adverse effect on our business, financial condition or results of operations and we may have exposure to liability for any resulting harm.

Risks Related to Our Intellectual Property

We may not be successful in obtaining or maintaining necessary rights to Synthetic Biotics, product candidates and processes for our development pipeline through acquisitions and in-licenses.

Presently, we have rights to certain intellectual property, through licenses from third parties and under patents and patent applications owned by us. The growth of our business will likely depend in part on our ability to obtain, maintain or enforce our and our licensors' intellectual property rights and to acquire or in-license additional proprietary rights. For example, our programs may involve additional product candidates or delivery systems that may require the use of additional proprietary rights held by third parties.

Our ultimate product candidates may also require specific formulations to work effectively and efficiently. These formulations may be covered by intellectual property rights held by others. We may be unable to acquire or in-license any relevant third-party intellectual property rights that we identify as necessary or important to our business operations.

In addition, our product candidates may require specific formulations to work effectively and efficiently, and these rights may be held by other third parties. We may be unable to develop, acquire or in-license compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of other companies may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These companies could have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, we have previously and may continue to collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such right of first negotiation for intellectual property, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to it. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

We intend to rely on patent rights and the status of our product candidates, if approved, as biologics eligible for exclusivity under the Biologics Price Competition and Innovation Act (BPCIA). If Synlogic is unable to obtain or maintain exclusivity from the combination of these approaches, Synlogic may not be able to compete effectively in our markets.

We rely or will rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect the intellectual property related to our technologies and product candidates. Our success depends in large part on our and our licensors' ability to obtain regulatory exclusivity and maintain patent and other intellectual property protection in the United States and in other countries with respect to our proprietary technology and products.

We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates that are important to our business. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unsolved. The patent applications that we own, or in-license may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue, and even if such patents cover our product candidates, third parties may challenge their validity, enforceability, or scope, which may result in such patents being narrowed, found unenforceable or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates, or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

We, independently or together with our licensors or collaborators, have filed several patent applications covering various aspects of our product candidates. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

Even if we cannot obtain and maintain effective protection of exclusivity from our regulatory efforts and intellectual property rights, including patent protection, data exclusivity or orphan drug exclusivity, for our product candidates, we believe that our product candidates will be protected by exclusivity that prevents approval of a biosimilar in the United States for a period of twelve years from the time the product to which it claims similarity was first approved. However, The Biologics Price Competition and Innovation Act

of 2009, Title VII, Subtitle A of the Patent Protection and Affordable Care Act, Pub.L.No.111-148, 124 Stat.119, Sections 7001-02 signed into law March 23, 2010, and codified in 42 U.S.C. §262 (the BPCIA), created an elaborate and complex patent dispute resolution mechanism for biosimilars that could prevent us from launching our product candidates in the United States or could substantially delay such launches. Current biosimilars litigation are addressing certain requirements of the BPCIA which is creating uncertainty over how certain terms of the BPCIA should be construed and this, presents uncertainty for both the biologics innovator and biosimilar party. The BPCIA mechanism required for biosimilar applicants may pose greater risk that patent infringement litigation will disrupt our activities and add increased expenses as well as divert management's attention. If a biosimilar version of one of our product candidates were approved in the United States, it could have a negative effect on our business.

We may not have sufficient patent term protections for our product candidates to effectively protect our business.

Patents have a limited term. In the United States, the statutory expiration of a patent is generally 20 years after it is filed. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product candidate, we may be open to competition. In addition, upon issuance in the United States any patent term can be adjusted based on specified delays caused by the applicant(s) or the USPTO.

Patent term extensions under the Hatch-Waxman Act in the United States and under supplementary protection certificates in Europe may be available to extend the patent or data exclusivity terms of our product candidates. We will likely seek patent term extensions, and we cannot provide any assurances that any such patent term extensions will be obtained and, if so, for how long. As a result, we may not be able to maintain exclusivity for our product candidates for an extended period after regulatory approval, if any, which would negatively impact our business, financial condition, results of operations and prospects. If we do not have sufficient patent terms or regulatory exclusivity to protect our product candidates, our business and results of operations will be adversely affected.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products, and recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

As is the case with other biotechnology companies, our success is heavily dependent on patents. Obtaining and enforcing patents in the biotechnology industry involves both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in specified circumstances and weakened the rights of patent owners in specified situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

If we are unable to maintain effective proprietary rights for our product candidates or any future product candidates, we may not be able to compete effectively in our proposed markets.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent. We also utilize processes for which patents are difficult to enforce. In addition, other elements of our products, and many elements of our product candidate discovery and development processes involve proprietary know-how, information or technology that is not covered by patents. Trade secrets may be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, collaborators, advisors, independent contractors or other third parties. We also seek to preserve the integrity and confidentiality of our data and trade secrets, including by maintaining physical and electronic security of our premises and our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, or misappropriation of our intellectual property by third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results, and financial condition.

Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, collaborators, advisors, independent contractors and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques.

Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business, financial condition or results of operations. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technology without infringing the patent rights of third parties. Numerous third-party U.S. and non-U.S. issued patents and pending applications exist in the area of Synthetic Biotics. We are aware of U.S. and foreign patents and pending patent applications owned by third parties that cover similar therapeutic uses as the product candidates we are developing. We are currently monitoring these patents and patent applications. We may in the future pursue available proceedings in the U.S. and foreign patent offices to challenge the validity of these patents and patent applications. In addition, or alternatively, we may consider whether to seek to negotiate a license of rights to technology covered by one or more of such patents and patent applications. If any patents or patent applications cover our product candidates or technologies, we may not be free to manufacture or market our product candidates as planned, absent such a license, which may not be available to us on commercially reasonable terms, or at all.

It is also possible that we have failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000 and applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patents may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to specified limitations, be later amended in a manner that could cover our technologies, our product candidates or the use of our product candidates.

There have been many lawsuits and other proceedings filed by third parties involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, and reexamination, post-grant review and equivalent proceedings before the USPTO and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We depend, in part, on our licensors to file, prosecute, maintain, defend and enforce patents and patent applications that are material to our business.

While we normally seek and gain the right to fully prosecute the patent applications relating to our product candidates, there may be times when the patent applications enabling our product candidates are controlled by our licensors. If any of our existing or future licensors fail to appropriately and broadly prosecute and maintain patent protection for patents covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using, importing, and selling competing products. In addition, even where we now have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors in effect from actions prior to us assuming control over patent prosecution.

If we fail to comply with obligations in the agreements under which we license intellectual property and other rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to certain intellectual property license agreements and expect to enter into additional license agreements in the future. Our existing agreements impose, and future license agreements may impose, certain obligations, including the payment of milestones and royalties based on revenues from sales of our products utilizing the technologies licensed from our licensors, and such obligations could adversely affect the overall profitability for us of any products that we may seek to commercialize. In addition, we

will need to outsource and rely on third parties for many aspects of the clinical development, sales and marketing of our product candidates covered under our license agreements. Delay or failure by these third parties could adversely affect the continuation of our license agreements with our third-party licensors. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, these agreements may be subject to termination by the licensor which could have a material adverse effect on our business.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To cease such infringement or unauthorized use, we or one of our licensing partners may be required to file patent infringement claims against a third-party to enforce one of our patents which can be expensive, time-consuming and unpredictable. In addition, in an infringement proceeding or a declaratory judgment action against us, a court may decide that one or more of our patents is not valid or is unenforceable or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

If we or one of our licensing partners were to initiate legal proceedings against a third-party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third-party can assert invalidity or unenforceability of a patent. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description, clarity or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or other jurisdictions, even outside the context of litigation. Such mechanisms include re-examination, inter partes review, post-grant review and equivalent proceedings in foreign jurisdictions, such as opposition or derivation proceedings. Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity, unpatentability and/or unenforceability, we may lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions or correct inventorship with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to us from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation, derivation or interference proceedings may result in a decision adverse to our interests and, even if successful, may result in substantial costs and distract our management and other employees. In addition, we may be unable to raise the funds necessary to conduct our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. Any disclosure of confidential information could adversely affect our business. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may in the future be subject to claims that former employees, consultants, collaborators, advisors, independent contractors or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor or other claims challenging the inventorship of our patents or ownership of our intellectual property (including patents and intellectual property that we in-license). Therefore, our rights to these patents may not be exclusive and third parties, including competitors, may have access to intellectual property that is important to our business. In addition, co-owners from whom we do not yet have a license or assignment may raise claims surrounding inventorship or ownership of patents that ultimately issue from this patent family, potentially resulting in issued patents to which we would not have rights under our existing license agreements. Further, in jurisdictions outside the United States, a license may not be enforceable unless all the owners of the intellectual property agree or consent to the license. In addition,

we may have inventorship disputes arising from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship of our patents. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may be subject to claims that our employees, consultants, collaborators, advisors, independent contractors or other third parties have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at universities, academic research institutions and at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we have written agreements with and make every effort to ensure that our employees, consultants, collaborators, advisors, independent contractors or other third parties do not use the proprietary information or intellectual property rights of others in their work for us, we may in the future be subject to claims that our employees, consultants, collaborators, advisors, independent contractors or other third parties have inadvertently or intentionally used or disclosed confidential information of these third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

We have limited intellectual property rights outside the United States. Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and intellectual property rights in some countries outside the United States can have a different scope and strength and be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties (including competitors) from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but where enforcement rights are not as strong as those in the United States. 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.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of some countries, particularly some developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult in those jurisdictions for us to stop the infringement or misappropriation of our patents or other intellectual property rights, or the marketing of competing products in violation of our proprietary rights. Proceedings to enforce our patents and other intellectual property rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, such proceedings could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly and could put our patent applications at risk of not issuing and could provoke third parties to assert claims of infringement or misappropriation 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. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

If our trademarks and trade names are not adequately protected, we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We have filed for trademark registration of certain marks relating to our current branding. If our trademarks and trade names are not adequately protected, we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and establish name recognition based on our trademarks and trade names, then we may not be able to

compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Risks Related to Our Reliance on Third Parties

We rely, and expect to continue to rely, on third parties to conduct some aspects of our product formulation, research, preclinical, and clinical studies, and those third parties may not perform satisfactorily, including by failing to meet deadlines for the completion of such formulation, research or testing.

We have relied upon and plan to continue to rely upon third parties, including independent clinical investigators, contracted laboratories and third-party CROs, to conduct our preclinical studies and clinical trials, as well as certain product candidate discovery and development activities, in accordance with applicable regulatory requirements and to monitor and manage data for our ongoing preclinical and clinical programs. We rely on these parties for execution of our preclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third-party contractors and CROs are required to comply with good laboratory practices (GLP), as applicable, and good clinical practice (GCP) requirements, which are regulations and guidelines enforced by the FDA, the EMA and other comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce these GLP and GCP through periodic inspections of laboratories conducting GLP studies, and clinical trial sponsors, principal investigators, CROs, and trial sites when auditing for GCP compliance. If we, our investigators or any of our CROs or contracted laboratories fail to comply with applicable GLP and GCP, as applicable, the data generated in our preclinical studies and clinical trials may be deemed unreliable and the FDA, the EMA or other comparable foreign regulatory authorities may require us to perform additional preclinical studies or clinical trials before approving our marketing applications for our therapeutic product candidates. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our preclinical studies or clinical trials comply with applicable GLP or GCP regulations. In addition, our clinical trials must be conducted with product produced in compliance with applicable cGMP regulations. Our failure to comply with these regulations may require us to repeat preclinical studies or clinical trials, which would delay the regulatory approval process.

Further, these laboratories, investigators and CROs are not our employees, and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our product candidates and clinical trials. If independent laboratories, investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if their performance is substandard, it may delay or compromise the prospects for approval and commercialization of any product candidates that we develop. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated.

There is a limited number of third-party service providers that specialize or have the expertise required to achieve our business objectives. If any of our relationships with these third-party laboratories, CROs or clinical investigators terminate, we may not be able to enter into arrangements with alternative laboratories, CROs or investigators or to do so in a timely manner or on commercially reasonable terms. If laboratories, CROs or clinical investigators do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our preclinical or clinical protocols, regulatory requirements or for other reasons, our preclinical studies or clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional laboratories or CROs (or investigators) involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new laboratory or CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our contracted laboratories and CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and results of operations.

In addition, clinical investigators may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the preclinical study or clinical trial, the integrity of the data generated at the applicable preclinical study or clinical trial site may be questioned and the utility of the preclinical study or clinical trial itself may be jeopardized, which could result in the delay or rejection by the FDA. Any such delay or rejection could prevent us from commercializing our clinical-stage product candidate or any future therapeutic product candidates it may develop.

We rely on third-party supply and manufacturing partners for drug supplies for our late-stage clinical activities and may do the same for any commercial supplies of our product candidates.

We rely on third-party supply and manufacturing partners to supply the materials and components to manufacture late-stage clinical trial drug supplies. We have not yet manufactured or formulated any product candidate on a commercial scale and may not be able to do so for any of our product candidates. We will work to develop and optimize our manufacturing process, and we cannot be sure that the process will result in therapies that are safe, potent, effective, or in an amount that satisfies our commercial needs.

We have agreements with Azzur Cleanrooms-On-Demand to lease clean-room space at their facility for manufacturing and formulation of cGMP material for our clinical trials and we have agreed to pay Azzur to renovate and upgrade the cleanroom space for expanded use. If Azzur were to not adhere to our agreement or suffer a material adverse event that affected their delivery of services to us, our ability to conduct clinical operations would be impacted.

There can be no assurance that our supply of research and development, preclinical and clinical development drugs and other materials will not be limited, interrupted, restricted in certain geographic regions or of satisfactory quality or continue to be available at acceptable prices. In particular, any replacement of any product formulation manufacturer we may engage could require significant effort and expertise because there may be a limited number of qualified replacements.

Synthetic Biotics are complex and difficult to manufacture. We could experience production or technology transfer problems that result in delays in our development or commercialization schedules or otherwise adversely affect our business. Issues with the manufacturing process, even minor deviations from the normal process, could result in insufficient yield, product deficiencies or manufacturing failures that result in lot failures, insufficient inventory, and product recalls.

Many factors common to the manufacturing of most biologics and drugs could also cause production interruptions, including raw materials shortages, raw material failures, growth media failures, equipment malfunctions, facility contamination, labor problems, natural disasters, disruption in utility services, terrorist activities, or acts of God beyond our control. We also may encounter problems in hiring and retaining the experienced specialized personnel needed to operate our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing processes or facilities could make us a less attractive collaborator for academic research institutions and other parties, which could limit our access to additional attractive development programs, result in delays in our clinical development or marketing schedules and harm our business.

The manufacturing process for a product candidate is subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMP regulations. Any of our suppliers or manufacturers could fail to comply with such requirements or to perform our obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials could become limited or interrupted for other reasons. Under these circumstances, we may choose or be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, manufacture in collaboration with a third-party at their facilities, or enter into an agreement with another third-party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from transferring such skills or technology to another third-party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third-party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines and may be required to conduct bridging studies or repeat clinical trials to assure comparable safety, purity and potency. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We may rely on third-party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third-party's failure to execute on our manufacturing requirements could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of product candidates under development, which may impact our potential economic benefits;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of a collaborator;

- subjecting our product candidates to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

We enter into various contracts in the normal course of our business in which we indemnify the other party to the contract. In the event we have to perform under these indemnification provisions, it could have a material adverse effect on our business, financial condition and results of operations.

In the normal course of business, we periodically enter into academic, commercial, service, collaboration, licensing, consulting and other agreements that contain indemnification provisions. With respect to our academic and other research agreements, we typically indemnify the institution and related parties from losses arising from claims relating to the products, processes or services made, used, sold or performed pursuant to the agreements for which we have secured licenses, and from claims arising from our or our sublicensees' exercise of rights under the agreement. With respect to our collaboration agreements, we typically indemnify our collaborators from any third-party product liability claims that could result from the production, use or consumption of the product, as well as for alleged infringements of any patent or other intellectual property right by a third-party. With respect to consulting agreements, we indemnify consultants from claims arising from the good faith performance of their services.

Should our obligation under an indemnification provision exceed applicable insurance coverage or should we be denied insurance coverage, our business, financial condition and results of operations could be adversely affected. Similarly, if we are relying on a collaborator to indemnify us and the collaborator is denied insurance coverage or the indemnification obligation exceeds the applicable insurance coverage, and if the collaborator does not have other assets available to indemnify us, our business, financial condition and results of operations could be adversely affected.

To the extent we are able to enter into collaborative arrangements or strategic alliances, we may be exposed to risks related to those collaborations and alliances.

Biotechnology companies sometimes become dependent upon collaborative arrangements or strategic alliances to complete the development and commercialization of product candidates. If we elect to enter into collaborative arrangements or strategic alliances, these arrangements may place the development of our product candidates outside our control, may require us to relinquish important rights or may otherwise be on terms unfavorable to us.

Dependence on collaborative arrangements or strategic alliances would subject us to a number of risks, including the risk that:

- we may not be able to control the amount and timing of resources that our collaborators may devote to the relevant product candidates;
- our collaborators may experience financial difficulties;
- we may be required to relinquish important rights, such as marketing and distribution rights;
- business combinations or significant changes in a collaborator's business strategy may also adversely affect a collaborator's willingness or ability to complete our obligations under any arrangement;
- a collaborator could independently move forward with a competing drug candidate developed either independently or in collaboration with others, including our competitors; and
- collaborative arrangements are often terminated or allowed to expire, which would delay the development and may increase the cost of developing our drug candidates.

We may attempt to form collaborations in the future with respect to our product candidates, but we may not be able to do so, which may cause us to alter our development and commercialization plans.

We may attempt to form strategic collaborations, create joint ventures or enter into licensing arrangements with third parties with respect to our programs or platform that we believe will complement or augment our existing business. We may face significant competition in seeking appropriate strategic collaborators, and the negotiation process to secure appropriate terms is time consuming and complex. We may not be successful in our efforts to establish such a strategic collaboration for any product candidates and programs on terms that are acceptable to us, or at all. This may be because our product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort, our research and development pipeline may be viewed as insufficient, the competitive or intellectual property landscape may be viewed as too intense or risky, and/or third parties may not view our product candidates and programs as having sufficient potential for commercialization, including the likelihood of an adequate safety and efficacy profile.

Any delays in identifying suitable collaborators and entering into agreements to develop and/or commercialize our product candidates could delay the development or commercialization of our product candidates, which may reduce their competitiveness even if they reach the market. Absent a strategic collaborator, we would need to undertake development and/or commercialization activities at our own expense. If we elect to fund and undertake development and/or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we are unable to do so, we may not be able to develop our product candidates or bring them to market and our business may be materially and adversely affected.

Risks Related to Commercialization of Our Product Candidates

If any of our product candidates is approved for marketing and commercialization and we are unable to develop sales, marketing and distribution capabilities on our own or enter into agreements with third parties to perform these functions on acceptable terms, we will be unable to successfully commercialize any such future products.

We currently have no sales, marketing or distribution capabilities or experience. If any of our product candidates is approved for marketing and commercialization, we will need to develop internal sales, marketing and distribution capabilities to commercialize such products, which would be expensive and time-consuming, or enter into collaborations with third parties to perform these services. If we decide to market our products directly, we will need to commit significant financial and managerial resources to develop a marketing and sales force with technical expertise and supporting distribution, administration and compliance capabilities. If we rely on third parties with such capabilities to market our products or decide to co-promote products with collaborators, we will need to establish and maintain marketing and distribution arrangements with third parties, and there can be no assurance that we will be able to enter into such arrangements on acceptable terms or at all. In entering into third-party marketing or distribution arrangements, any revenue we receive will depend upon the efforts of third parties and there can be no assurance that such third parties will establish adequate sales and distribution capabilities or be successful in gaining market acceptance of any approved product. If we are not successful in commercializing any product approved for marketing and commercialization in the future, either on our own or through third parties, our business, financial condition, results of operations and prospects may be adversely affected.

If the market opportunities for our product candidates are smaller than we believe they are, we may not meet our revenue expectations and, assuming approval of a product candidate, our business may suffer. Because the patient populations in the market for our product candidates may be small, we must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth.

Given the small number of patients who have the diseases that we are targeting, our eligible patient population and pricing estimates may differ significantly from the actual market addressable by our product candidates. Our projections of both the number of people who have applicable diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, patient foundations, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our business, financial condition, results of operations and prospects.

We face substantial competition and our competitors may discover, develop or commercialize products faster or more successfully than us.

The development and commercialization of new products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, universities and other research institutions worldwide with respect to our product candidates that we may seek to develop or commercialize in the future. For example, BioMarin, Inc., Nestlé Health Science S.A. (Codexis, Inc.), Homology Medicines, Inc., American Gene Technologies International Inc., Generation Bio Co., Agios Pharmaceuticals, Inc., SOM Biotech SL, Jnana Therapeutics and other discovery stage companies have developed or are developing product candidates for the treatment of PKU. Novome Biotechnologies, Inc., Federation Bio, Inc., Oxidien Pharmaceuticals L.L.C. and others are developing product candidates for enteric hyperoxaluria. Aeglea BioTherapeutics and Travere Therapeutics are both developing product candidates for HCU. Our competitors may succeed in developing, acquiring or licensing technologies and products that are more effective or less costly than the product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete and noncompetitive. In addition to the competition, we face from alternative therapies for the diseases we intend to target with our product candidates, we are also aware of several companies that are also working specifically to develop engineered bacteria as cellular drug therapies, such as Precigen, Inc. Further there are several companies working to develop other similar products. Third-party payors, including governmental and private insurers, may also encourage the use of generic products.

If our competitors obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than us, it could result in our competitors establishing a strong market position before we are able to enter the market.

Many of our competitors have materially greater name recognition and substantially greater financial, manufacturing, marketing, research and drug development resources than we do. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Large pharmaceutical companies in particular have extensive expertise in preclinical and clinical testing and in obtaining regulatory approvals for drugs. In addition, academic institutions, government agencies, and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaborative or licensing relationships with our competitors. Failure of our product candidates to effectively compete against established treatment options or in the future with new products currently in development would harm our business, financial condition, results of operations and prospects.

The commercial success of any of our current or future product candidates will depend upon the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community.

Even with approvals from the FDA and comparable foreign regulatory authorities, the commercial success of our products will depend in part on the health care providers, patients, and third-party payors accepting our product candidates as medically useful, cost-effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients and third-party payors. The degree of market acceptance of any of our products will depend on a number of factors, including but not limited to:

- the efficacy of the product as demonstrated in clinical trials and potential advantages over competing treatments;
- the safety and side effect profile of the product as demonstrated in clinical trials and potential advantages over competing treatments;
- the prevalence and severity of the disease targeted;
- the clinical indications for which approval is granted, including any limitations or warnings contained in a product's approved labeling;
- the convenience and ease of administration;
- the cost of treatment;
- the willingness of the patients and physicians to accept products engineered from bacteria and these therapies;
- the perceived ratio of risk and benefit of these therapies by physicians, patients, and payers, and the willingness of physicians to recommend these therapies to patients based on such risks and benefits;
- the marketing, sales and distribution support for the product;
- the publicity concerning the products or competing products and treatments; and
- the pricing and availability of third-party insurance coverage and reimbursement.

Even if a product displays a favorable efficacy and safety profile upon approval, market acceptance of the product remains uncertain. Efforts to educate the medical community and third-party payors on the benefits of the products may require significant investment and resources and may never be successful. If our products fail to achieve an adequate level of acceptance by physicians, patients, third-party payors, and other health care providers, we will not be able to generate sufficient revenue to become or remain profitable.

We may not be successful in any efforts to identify, license, discover, develop, or commercialize additional product candidates.

Although a substantial amount of our effort will focus on the clinical testing, potential approval, and commercialization of our existing product candidates, the success of our business is also expected to depend in part upon our ability to identify, license, discover, develop, or commercialize additional product candidates. Research programs to identify new product candidates require substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product

candidates that ultimately prove to be unsuccessful. Our research programs or licensing efforts may fail to yield additional product candidates for clinical development and commercialization for a number of reasons, including but not limited to the following:

- our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates;
- we may not be able or willing to assemble sufficient resources to acquire or discover additional product candidates;
- our product candidates may not succeed in preclinical or clinical testing;
- our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may be covered by third parties' patents or other exclusive rights;
- the market for a product candidate may change during development or commercialization so that such a product may become unreasonable to continue to develop or commercialize;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by patients, the medical community, or third-party payors.

If any of these events occur, we may be forced to abandon our development efforts for one or more product candidates, or we may not be able to identify, license, discover, develop, or commercialize additional product candidates, which would have a material adverse effect on our business, financial condition or results of operations and could potentially cause us to cease operations.

Failure to obtain or maintain adequate reimbursement or insurance coverage for products, if any, could limit our ability to market those products and decrease our ability to generate revenue.

The pricing, coverage, and reimbursement of our approved products, if any, must be sufficient to support our commercial efforts and other development programs and the availability and adequacy of coverage and reimbursement by third-party payors, including governmental and private insurers, are essential for most patients to be able to afford expensive treatments. Sales of our approved products, if any, will depend substantially, both domestically and abroad, on the extent to which the costs of our approved products, if any, will be paid for or reimbursed by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or government payors and private payors. If coverage and reimbursement are not available, or are available only in limited amounts, we may have to subsidize or provide products for free or we may not be able to successfully commercialize our products.

In addition, there is significant uncertainty related to the insurance coverage and reimbursement for newly approved products. In the United States, the principal decisions about coverage and reimbursement for new drugs are typically made by the Centers for Medicare & Medicaid Services (CMS), an agency within the HHS, as CMS decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for novel product candidates such as ours and what reimbursement codes our product candidates may receive if approved. No uniform policy for coverage and reimbursement for drug products exist among third-party payors in the United States. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic/biosimilar drug or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidate and other therapies as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidate over other available and comparable products, pricing of existing drugs may limit the amount we will be able to charge for its product candidate. These payors may deny or revoke the reimbursement status of a given drug product or establish prices for new or existing marketed products at levels that are too low to enable it to realize an appropriate return on our investment in product development. If coverage and reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates and may not be able to obtain a satisfactory financial return on products that we may develop.

For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. For example, under these circumstances, physicians may limit how much or under what circumstances they will prescribe or administer our products and patients may deliver to purchase such products. This, in turn, could affect our ability to commercialize our products successfully and impact our profitability, results of operations, financial condition, and future success.

Outside the United States, international operations are generally subject to extensive governmental price controls and other price-restrictive regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of products. In many countries, the prices of products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products but monitor and control company profits. Price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our products, if any. Accordingly, in markets outside the United States, the potential revenue from the sale of our products may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and private payors in the United States and abroad to limit or reduce healthcare costs may result in restrictions on coverage and the level of reimbursement for new products and, as a result, they may not cover or provide adequate payment for our products. We expect to experience pricing pressures in connection with products due to the increasing trend toward managed healthcare, including the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs has, and is expected to continue to increase in the future. As a result, profitability of our products, if any, may be more difficult to achieve even if they receive regulatory approval.

Risks Related to Our Business Operations and Employees

Our failure to attract and retain senior management and key scientific personnel may prevent us from successfully developing our product candidates or any future product candidate, conducting our clinical trials and commercializing any products.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We believe that our future success is highly dependent upon the contributions of our senior management, particularly our president and chief executive officer, as well as our senior scientists and other members of our senior management team. The loss of services of any of these individuals could delay or prevent the successful development of our product pipeline, completion of our planned clinical trials or the commercialization of the products we develop.

Although we have not historically experienced significant difficulties attracting and retaining qualified employees, we could experience such problems in the future. For example, competition for qualified personnel in the biotechnology and pharmaceuticals field is intense due to the limited number of individuals who possess the skills and experience required by our industry. We will need to hire additional personnel as we expand our clinical development and commercial activities. We may not be able to attract and retain quality personnel on acceptable terms, or at all.

Our employees, independent contractors, principal investigators, CROs, consultants and collaborators may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, independent contractors, consultants and collaborators may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate: (1) regulations of regulatory authorities in jurisdictions where we are performing activities in relation to our product candidates, including those laws requiring the reporting of true, complete and accurate information to such authorities; (2) manufacturing regulations and standards; (3) fraud and abuse and anti-corruption laws and regulations; or (4) laws that require the reporting of true and accurate financial information and data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, bias, misconduct, kickbacks, self-dealing and other abusive practices, and these laws may differ substantially from country to country. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. These activities also include the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting ourselves from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending itself or asserting our rights, those actions could have a significant impact on our business including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in subsidized healthcare programs in a given country, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Related to Our Common Stock

Our principal stockholders and management own a significant percentage of our stock and are able to exert significant control over matters subject to stockholder approval.

Based on the beneficial ownership of our common stock as of November 3, 2022, our executive officers and directors, together with holders of 5% or more of our common stock outstanding and their respective affiliates, beneficially own approximately 48.4% of our common stock. Accordingly, these stockholders have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, consolidation or sale of all or substantially all of our assets or any other significant corporate transaction. The interests of these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could delay or prevent a change of control, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of the company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

Future sales of our common stock or securities convertible or exchangeable for our common stock may depress our stock price.

If our existing stockholders or holders of our options sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. The perception in the market that these sales may occur could also cause the trading price of our common stock to decline. As of November 3, 2022, there were a total of 70,519,940 shares of our common stock outstanding.

Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of our operating expenses;
- receipt, modification or termination of government contracts or grants, and the timing of payments we receive under these arrangements;
- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make under these arrangements; and
- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of the company's stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Provisions of our charter documents or Delaware law could delay or prevent an acquisition of us, even if the acquisition would be beneficial to our stockholders and could make it more difficult for you to change management.

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control that our stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. In addition, these provisions may frustrate or prevent any attempt by our stockholders to replace or remove our current management by making it more difficult to replace or remove our Board of Directors. These provisions include:

- a classified board of directors so that not all directors are elected at one time;
- a prohibition on stockholder action through written consent;
- no cumulative voting in the election of directors;
- the exclusive right of our Board of Directors to elect a director to fill a vacancy created by the expansion of our Board of Directors or the resignation, death or removal of a director;
- a requirement that special meetings of our Stockholders be called only by our Board of Directors, the chairman of our Board of Directors, the chief executive officer or, in the absence of a chief executive officer, the president;

- an advance notice requirement for stockholder proposals and nominations;
- the authority of our Board of Directors to issue preferred stock with such terms as our Board of Directors may determine; and
- a requirement of approval of not less than 66 2/3% of all outstanding shares of our capital stock entitled to vote to amend any bylaws by stockholder action, or to amend specific provisions of our certificate of incorporation.

In addition, Delaware law prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person who, together with its affiliates, owns or within the last three years has owned 15% or more of the company's voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. Accordingly, Delaware law may discourage, delay or prevent a change in control of the company.

In addition, our amended and restated certificate of incorporation, to the fullest extent permitted by law, provides that the Court of Chancery of the State of Delaware will be the exclusive forum for: any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, or the DGCL, our amended and restated certificate of incorporation, or our amended and restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. This exclusive forum provision does not apply to suits brought to enforce a duty or liability created by the Exchange Act. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision and asserts claims under the Securities Act, inasmuch as Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rule and regulations thereunder. There is uncertainty as to whether a court would enforce such provision with respect to claims under the Securities Act, and our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find the choice of forum provisions contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, results of operations and financial condition.

Provisions in our charter and other provisions of Delaware law could limit the price that investors are willing to pay in the future for shares of our common stock.

We do not anticipate paying any cash dividends on our common stock in the foreseeable future; therefore, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

We have never declared or paid cash dividends on our common stock. We do not anticipate paying any cash dividends on our common stock in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund our operations. In addition, the terms of any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrade our common stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. In addition, if our operating results fail to meet the forecast of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our common stock could decrease, which might cause our stock price and trading volume to decline.

Changes in, or interpretations of, accounting rules and regulations could result in unfavorable accounting charges or require us to change our compensation policies.

Accounting methods and policies for biopharmaceutical companies, including policies governing revenue recognition, research and development and related expenses and accounting for stock-based compensation, are subject to further review, interpretation and guidance from relevant accounting authorities, including the SEC. Changes to, or interpretations of, accounting methods or policies may require us to reclassify, restate or otherwise change or revise our financial statements, including those contained in this periodic report.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.

None.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

None.

Item 6. Exhibits.

EXHIBIT INDEX

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
31.1	Certification of Chief Executive Officer required by Rule 13a-14(a) or Rule 15d-14(a).	X			
31.2	Certification of Interim Chief Financial Officer required by Rule 13a-14(a) or Rule 15d-14(a).	X			
32.1*	Certification required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350).	X			
32.2*	Certification required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350).	X			
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Date File because XBRL tags are embedded within the Inline XBRL document.	X			
101.SCH	Inline XBRL Taxonomy Extension Schema Document	X			
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	X			
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	X			
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	X			

(*) The certifications attached as Exhibit 32.1 and Exhibit 32.2 that accompany this Quarterly Report on Form 10-Q are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of Synlogic, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of such Form 10-Q), irrespective of any general incorporation language contained in such filing.

SIGNATURES

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

Date: November 10, 2022

SYNLOGIC, INC.

By: /s/ AOIFE BRENNAN
Aoife Brennan
President and Chief Executive Officer
(Principal Executive Officer)

By: /s/ MICHAEL JENSEN
Michael Jensen
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

EXHIBIT 31.1

CERTIFICATION PURSUANT
TO RULES 13a-14(a) OR 15d-14(a) UNDER
THE SECURITIES EXCHANGE ACT OF 1934

I, Aoife Brennan, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Synlogic, Inc. (the "registrant");

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 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.

Date: November 10, 2022

/s/ AOIFE BRENNAN

Aoife Brennan
President and Chief Executive Officer
(Principal Executive Officer)

EXHIBIT 31.2

CERTIFICATION PURSUANT
TO RULES 13a-14(a) OR 15d-14(a) UNDER
THE SECURITIES EXCHANGE ACT OF 1934

I, Michael Jensen, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Synlogic, Inc. (the "registrant");

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 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.

Date: November 10, 2022

/s/ MICHAEL JENSEN
Michael Jensen
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

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 of Synlogic, Inc. (the "Company") on Form 10-Q for the period ended September 30, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Aoife Brennan, President and Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to my knowledge that:

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

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

/s/ AOIFE BRENNAN

Aoife Brennan
President and Chief Executive Officer
(Principal Executive Officer)

November 10, 2022

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 of Synlogic, Inc. (the "Company") on Form 10-Q for the period ended September 30, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Michael Jensen, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to my knowledge that:

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

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

/s/ MICHAEL JENSEN

Michael Jensen
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

November 10, 2022

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.