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 June 30, 2019

or

☐ **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: 001-38756

SYNTHORX, INC.

(Exact name of registrant as specified in its charter)

Delaware	**46-4709185**
(State of incorporation)	**(I.R.S. Employer Identification No.)**
11099 N. Torrey Pines Road, Suite 190 La Jolla, California	**92037**
(Address of principal executive offices)	**(Zip Code)**

(858) 750-4789
(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	THOR	The Nasdaq Global Select Market

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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 ☒

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of July 31, 2019 was 32,266,004.

SYNTHORX, INC.
QUARTERLY REPORT on FORM 10-Q

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PART I—FINANCIAL INFORMATION

ITEM 1. Financial Statements.

SYNTHORX, INC.
CONDENSED BALANCE SHEETS
(in thousands, except share and per share amounts)

	June 30, 2019	December 31, 2018
	(unaudited)	
Assets		
Current Assets:		
Cash and cash equivalents	$ 23,534	$ 188,356
Investment securities, available-for-sale	141,644	—
Prepaid expenses and other current assets (including related party amounts of $0 and $28, respectively)	3,554	1,688
Total current assets	168,732	190,044
Operating lease right-of-use asset (including related party amounts of $2,013 and $0, respectively)	3,003	—
Property and equipment, net	1,628	1,382
Other assets	30	80
Total assets	$ 173,393	$ 191,506
Liabilities and Stockholders' Equity		
Current Liabilities:		
Accounts payable	$ 884	$ 2,228
Accrued liabilities (including related party amounts of $274 and $123, respectively)	6,122	4,814
Lease liability, current (including related party amounts of $151 and $0, respectively)	403	—
Total current liabilities	7,409	7,042
Lease liability, noncurrent (including related party amounts of $1,974 and $0, respectively)	2,818	—
Deferred rent (including related party amounts of $0 and $72, respectively)	—	104
Total liabilities	10,227	7,146
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Common stock, $0.001 par value; authorized shares 200,000,000 at June 30, 2019 and December 31, 2018, respectively; issued shares — 32,263,757 and 32,103,953 at June 30, 2019 and December 31, 2018, respectively; outstanding shares— 31,711,124 and 31,394,830 at June 30, 2019 and December 31, 2018, respectively	32	31
Additional paid-in capital	255,605	253,807
Accumulated deficit	(92,699)	(69,478)
Accumulated other comprehensive income	228	—
Total stockholders' equity	163,166	184,360
Total liabilities and stockholders' equity	$ 173,393	$ 191,506

The accompanying notes are an integral part of these financial statements.

SYNTHORX, INC.
CONDENSED STATEMENTS OF OPERATIONS
(in thousands, except share and per share amounts)
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Operating expenses:				
Research and development (includes related party amounts of $358, $229, $598, and $499, respectively)	$ 10,425	$ 3,387	$ 19,989	$ 5,152
General and administrative (includes related party amounts of $76, $71, $158, and $136, respectively)	3,040	602	5,395	1,027
Total operating expenses	13,465	3,989	25,384	6,179
Loss from operations	(13,465)	(3,989)	(25,384)	(6,179)
Other income (expense):				
Change in fair value of preferred stock purchase right liability	—	(14)	—	(14)
Interest income, net	1,095	—	2,163	—
Net loss	$ (12,370)	$ (4,003)	$ (23,221)	$ (6,193)
Net loss per common share, basic and diluted	$ (0.39)	$ (4.21)	$ (0.74)	$ (6.54)
Weighted average common shares outstanding, basic and diluted	31,561,445	951,066	31,496,114	946,854

The accompanying notes are an integral part of these financial statements.

SYNTHORX, INC.
CONDENSED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Net loss	$ (12,370)	$ (4,003)	$ (23,221)	$ (6,193)
Other comprehensive gain:				
Unrealized gain on investment securities	192	—	228	—
Comprehensive loss	$ (12,178)	$ (4,003)	$ (22,993)	$ (6,193)

The accompanying notes are an integral part of these financial statements.

SYNTHORX, INC.
CONDENSED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY(DEFICIT)
(in thousands, except share data)
(Unaudited)

Six Months Ended June 30, 2019

	Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Other Comprehensive	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Deficit	Income	Equity
Balance at December, 31 2018	—	$ —	31,394,830	$ 31	$ 253,807	$ (69,478)	$ —	$ 184,360
Exercise of common stock options and vesting of early exercised common stock options	—	—	289,864	1	279	—	—	280
Share issuance under employee stock purchase plan	—	—	26,430	—	247	—	—	247
Stock-based compensation	—	—	—	—	1,272	—	—	1,272
Other comprehensive income	—	—	—	—	—	—	228	228
Net loss	—	—	—	—	—	(23,221)	—	(23,221)
Balance at June 30, 2019	—	$ —	31,711,124	$ 32	$ 255,605	$ (92,699)	$ 228	$ 163,166

Three Months Ended June 30, 2019

	Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Other Comprehensive	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Deficit	Income	Equity
Balance at March 31, 2019	—	$ —	31,442,454	$ 31	$ 254,442	$ (80,329)	$ 36	$ 174,180
Exercise of common stock options and vesting of early exercised common stock options	—	—	242,240	1	228	—	—	229
Share issuance under employee stock purchase plan	—	—	26,430	—	247	—	—	247
Stock-based compensation	—	—	—	—	688	—	—	688
Other comprehensive income	—	—	—	—	—	—	192	192
Net loss	—	—	—	—	—	(12,370)	—	(12,370)
Balance at June 30, 2019	—	$ —	31,711,124	$ 32	$ 255,605	$ (92,699)	$ 228	$ 163,166

Six Months Ended June 30, 2018

	Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Other Comprehensive	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Deficit	Income	Deficit
Balance at December 31, 2017	7,253,898	$ 16,103	935,723	$ 1	$ 340	$ (12,869)	$ —	$ (12,528)
Issuance of Series C preferred stock, net of $292 of issuance costs	8,118,108	21,391	—	—	—	—	—	—
Exercise of common stock options and vesting of founder shares	—	—	15,346	—	1	—	—	1
Stock-based compensation	—	—	—	—	88	—	—	88
Net loss	—	—	—	—	—	(6,193)	—	(6,193)
Balance at June 30, 2018	15,372,006	$ 37,494	951,069	$ 1	$ 429	$ (19,062)	$ —	$ (18,632)

Three Months Ended June 30, 2018

	Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Other Comprehensive	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Deficit	Income	Deficit
Balance at March 31, 2018	7,253,898	$ 16,103	951,069	$ 1	$ 367	$ (15,059)	$ —	$ (14,691)
Issuance of Series C preferred stock, net of $292 of issuance costs	8,118,108	21,391	—	—	—	—	—	—
Exercise of common stock options and vesting of founder shares	—	—	—	—	—	—	—	—
Stock-based compensation	—	—	—	—	62	—	—	62
Net loss	—	—	—	—	—	(4,003)	—	(4,003)
Balance at June 30, 2018	15,372,006	$ 37,494	951,069	$ 1	$ 429	$ (19,062)	$ —	$ (18,632)

The accompanying notes are an integral part of these financial statements.

SYNTHORX, INC.
CONDENSED STATEMENTS OF CASH FLOWS
(in thousands)
(Unaudited)

	Six Months Ended June 30,	
	2019	**2018**
Cash flows from operating activities		
Net loss	$ (23,221)	$ (6,193)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	1,272	88
(Amortization of premiums) and accretion of discounts on investment securities, net	(1,220)	—
Depreciation	194	91
Change in fair value of purchase right liability	—	14
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(1,894)	(120)
Prepaid expenses and other current assets—related parties	28	(88)
Accounts payable and accrued liabilities	(5)	1,172
Accounts payable and accrued liabilities—related parties	151	(275)
Deferred rent - related parties	—	44
Operating lease right-of-use assets and liabilities, net	74	—
Operating lease right-of-use assets and liabilities, net—related parties	40	—
Other assets	50	—
Net cash used in operating activities	(24,531)	(5,267)
Cash flows from investing activities		
Purchases of investment securities	(169,446)	—
Proceeds from maturities of investment securities	29,250	—
Purchases of property and equipment	(440)	(337)
Net cash used in investing activities	(140,636)	(337)
Cash flows from financing activities		
Proceeds from issuance of convertible preferred stock and Series C preferred stock purchase right liability, net of issuance costs	—	26,255
Proceeds from exercise of common stock options and stock issuances under the employee stock purchase plan	345	1
Net cash provided by financing activities	345	26,256
Net (decrease) increase in cash and cash equivalents	(164,822)	20,652
Cash and cash equivalents		
Beginning of period	188,356	3,661
End of period	$ 23,534	$ 24,313

The accompanying notes are an integral part of these financial statements.

1. Organization and Business

Synthorx, Inc. (the "Company") was incorporated in the state of Delaware in January 2014 and is based in San Diego, California. The Company is a clinical-stage biopharmaceutical company focused on prolonging and improving the lives of people with cancer and autoimmune disorders. The Company's platform technology expands the genetic code by adding a new DNA base pair and is designed to create optimized biologics, which the Company refers to as Synthorins.

The Company has incurred significant operating losses since inception and expects to incur operating losses for the foreseeable future as it pursues the clinical and preclinical development of its programs and product candidates. As the Company continues to incur losses, its transition to profitability will depend on the successful development, approval and commercialization of its product candidates and on the achievement of sufficient revenues to support its cost structure. The Company may never achieve profitability, and unless and until it does, will need to continue to raise additional capital to fund its operations.

2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed financial statements of the Company should be read in conjunction with the audited financial statements and notes thereto as of and for the year ended December 31, 2018 included in the Company's Annual Report on Form 10-K ("Annual Report") filed with the Securities and Exchange Commission (the "SEC") on March 12, 2019. The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP") for interim financial information and in accordance with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, since they are interim statements, the accompanying financial statements do not include all of the information and notes required by GAAP for complete financial statements. In the opinion of management, the accompanying financial statements reflect all adjustments (consisting of normal recurring adjustments) that are necessary for a fair statement of the financial position, results of operations, comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for the interim periods presented. Interim results are not necessarily indicative of results for a full year.

The preparation of the Company's financial statements requires it to make estimates and assumptions that impact the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in the Company's financial statements and accompanying notes. The most significant estimates in the Company's financial statements relate to accruals for research and development expenses and the valuation of equity awards. These estimates and assumptions are based on current facts, historical experience and various other factors believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities and the recording of expenses that are not readily apparent from other sources. Actual results may differ materially and adversely from these estimates.

Reverse Stock Split

On November 26, 2018, the Company effected a 1-for-1.60224 reverse stock split of its common stock. The par value and the authorized shares of the common stock were not adjusted as a result of the reverse stock split. The accompanying financial statements and notes to the financial statements give retroactive effect to the reverse stock split for all periods presented.

Cash and Cash Equivalents

The Company considers all highly liquid investments with maturities at the date of acquisition of three months or less to be cash equivalents. These investments may include money market funds, U.S. Government agencies, corporate debt securities and commercial paper.

Marketable Securities

Investments with maturities at the date of acquisition of more than three months are considered marketable securities. The Company determines the appropriate classification of its investments at the time of acquisition and reevaluates such determination at each balance sheet date. The Company has classified its investment holdings as available-for-sale, as the sale of such securities may be required prior to maturity to implement management strategies. The Company's investment policy sets minimum credit quality criteria and maximum maturity limits on its investments to provide for safety of principle, liquidity and a reasonable rate of return. Available-for-sale securities are recorded at fair value, based on current market valuations. Unrealized holding gains and losses on available-for-sale securities are excluded from earnings and are reported as a separate component of other comprehensive income (loss) until realized. Realized gains and losses are included in non-operating other income (expense) on the statement of operations and are derived using the specific identification method for determining the cost of the securities sold. During the periods presented, no realized gains or losses were recorded on the sale or maturity of the Company's marketable securities and no impairments to reduce the value of an available-for-sale equity security were taken. See Note 5 for further discussion.

Research and Development Expenses

All research and development costs are expensed in the period incurred. Research and development expenses primarily consist of services provided by contract organizations for clinical and preclinical development, salaries and related expenses for personnel, including stock-based compensation expense, outside service providers, facilities costs, fees paid to consultants and other professional services, license fees, depreciation and supplies used in research and development. Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the related goods or services are received.

Stock-Based Compensation

Stock options issued pursuant to the Company's 2018 Equity Incentive Plan (the "2018 Plan") and 2014 Equity Incentive Plan (the "2014 Plan") and option features associated with the rights to purchase shares pursuant to the Company's 2018 Employee Stock Purchase Plan (the "ESPP") are valued using the Black-Scholes option pricing model on the date of grant or subscription period. This option pricing model involves a number of estimates, including the expected term of an award or subscription period, the anticipated stock volatility and risk-free interest rates. Stock-based compensation expense is recognized using the straight-line method and is based on the value of the portion of stock awards that are ultimately expected to vest or the number of shares estimated to be issued pursuant to the ESPP.

The table below summarizes the total stock-based compensation expense included in the Company's condensed statements of operations for stock options and shares subject to purchase under the ESPP for the periods presented (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Research and development	$ 81	$ 33	$ 481	$ 49
General and administrative	607	29	791	39
	$ 688	$ 62	$ 1,272	$ 88

Recent Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board ("FASB") established Topic 842, *Leases*, by issuing Accounting Standards Update ("ASU") No. 2016-02, which requires leases to be recognized on the balance sheet and disclose key information about leasing arrangements. Topic 842 was subsequently amended by ASU No. 2018-01, *Land Easement Practical Expedient for Transition to Topic 842*; ASU No. 2018-10, *Codification Improvements to Topic 842, Leases*; and ASU No. 2018-11, *Targeted Improvements*. The new standard establishes a right-of-use ("ROU") model that requires a lessee to recognize a ROU asset and lease liability on the balance sheet for all leases with a term longer than 12 months. Leases will be classified as finance or operating, with classification affecting the pattern and classification of expense recognition in the income statement.

A modified retrospective transition approach is required for ASU 2016-02, applying the new standard to all leases existing at the date of initial application. An entity may choose to use either (1) its effective date or (2) the beginning of the earliest comparative period presented in the financial statements as its date of initial application. The Company adopted the new standard on January 1, 2019, and used the effective date as its date of initial application. Consequently, financial information will not be updated, and the disclosures required under the new standard will not be provided for dates and periods before January 1, 2019. Further, the Company

elected the 'package of practical expedients' which does not require the Company to reassess its prior conclusions about lease identification, lease classification and initial direct costs under the new standard. On adoption, the Company recognized operating liabilities associated with leases of $3.3 million and corresponding ROU assets of $3.2 million, based on the present value of the remaining minimum rental payments under current leasing standards for existing operating leases. See Note 8 for further discussion.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement: Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement,* which modifies the disclosure requirements for fair value measurements. The amendments relate to disclosures regarding unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and the narrative description of measurement uncertainty and are to be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments should be applied retrospectively to all periods presented upon their effective date. The amendments are effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years, and early adoption is permitted. The Company is currently evaluating the timing and impact of the adoption of this guidance on the Company's consolidated financial statements.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses: Measurement of Credit Losses on Financial Instruments*, which changes the impairment model for most financial assets and certain other instruments. For trade receivables and other instruments, entities will be required to use a new forward-looking expected loss model that generally will result in the earlier recognition of allowances for losses. For available-for-sale debt securities with unrealized losses, the losses will be recognized as allowances rather than as reductions in the amortized cost of the securities. This guidance is effective for annual reporting periods beginning after December 15, 2019, including interim periods within those years, with early adoption permitted only as of annual reporting periods beginning after December 15, 2018. The Company is currently evaluating the timing and impact of the adoption of this guidance on the Company's consolidated financial statements.

3. Net Loss Per Share

Basic net loss per share is computed by dividing the net loss by the weighted average number of common shares outstanding for the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common shares and dilutive common share equivalents outstanding for the period determined using the treasury-stock and if-converted methods. For purposes of this calculation, convertible preferred stock, stock options, employee stock purchase rights, and unvested common stock subject to repurchase are considered to be common stock equivalents but are not included in the calculations of diluted net loss per share for the periods presented as their effect would be antidilutive. The Company incurred net losses for all periods presented and there were no reconciling items for potentially dilutive securities. More specifically, at June 30, 2019 and 2018, convertible preferred stock, stock options, employee stock purchase rights, and unvested common stock subject to repurchase totaling approximately 4,800,000 shares and 17,500,000 shares, respectively, were excluded from the calculation of diluted net loss per share because to do so would be anti-dilutive.

4. Fair Value Measurements

The Company follows authoritative accounting guidance, which among other things, defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or non-recurring basis. Fair value is defined as an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability.

As a basis for considering such assumptions, the accounting guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1: Observable inputs such as quoted prices in active markets.

Level 2: Inputs, other than the quoted prices in active markets, that are observable either directly or indirectly.

Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

The carrying amounts of the Company's prepaid expenses and other current assets, accounts payable and accrued liabilities are generally considered to be representative of their fair value because of the short nature of these instruments. The Company's investments, which may include money market funds and available-for-sale investment securities consisting of U.S. Treasury notes, and high quality, marketable debt instruments of corporations and government sponsored enterprises, are measured at fair value in accordance with the fair value hierarchy.

Assets measured at fair value on a recurring basis at June 30, 2019 and December 31, 2018, consisted of the following (in thousands):

		Fair Value Measurements at Reporting Date Using:		
	Balance at June 30, 2019	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds[1]	$ 23,532	$ 23,532	$ —	$ —
Government-sponsored enterprise securities	9,005	9,005		
Commercial paper	97,859	—	97,859	—
Corporate debt securities	34,780	—	34,780	—
Total	$ 165,176	$ 32,537	$ 132,639	$ -

(1) Included within cash and cash equivalents on the Company's condensed balance sheet.

		Fair Value Measurements at Reporting Date Using:		
	Balance at December 31, 2018	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds[1]	$ 185,203	$ 185,203	$ —	$ —
Total	$ 185,203	$ 185,203	$ —	$ —

(1) Included within cash and cash equivalents on the Company's condensed balance sheet.

The Company determines the fair value of commercial paper and corporate bonds with the aid of valuations provided by third parties using proprietary valuation models and analytical tools. These valuation models and analytical tools use market pricing or prices for similar instruments that are both objective and publicly available, including matrix pricing or reported trades, benchmark yields, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids and/or offers. The Company validates the valuations received from its primary pricing vendors for its level 2 securities by examining the inputs used in that vendor's pricing process and determines whether they are reasonable and observable. The Company also compares those valuations to recent reported trades for those securities. The Company did not adjust any of the valuations received from these independent third parties with respect to any of its level 2 securities at June 30, 2019 and no transfers between levels occurred during the either of the reporting periods presented.

5. Investments in Marketable Securities

The Company's investment policy defines allowable investment securities and establishes guidelines relating to credit quality, diversification, and maturities of its investments to preserve principal and maintain liquidity. In accordance with the Company's investment policy, it has invested funds in marketable securities at June 30, 2019. The Company had no investments in marketable securities at December 31, 2018.

The cost, gross unrealized holding gains, gross unrealized holding losses and fair value of available-for-sale investments by types and classes of security at June 30, 2019 consisted of the following (in thousands):

		June 30, 2019				
	Maturity (in years)	Amortized Cost Basis	Other-than-temporary Impairments	Gross Unrealized Holding Gains	Gross Unrealized Holding Losses	Fair Value
Commercial paper	1 year or less	$ 97,704	$ —	$ 155	$ —	$ 97,859
Corporate debt securities	1 year or less	34,712	—	68	—	34,780
Government-sponsored enterprise securities	1 year or less	9,000	—	5	—	9,005
Total available-for-sale securities		$ 141,416	$ —	$ 228	$ —	$ 141,644

The Company reviews its investments to identify and evaluate investments that have an indication of possible other-than-temporary impairment. Factors considered in determining whether a loss is other-than-temporary include the length of time and extent to which fair value has been less than the cost basis, the financial condition and near-term prospects of the investee, and the Company's intent and ability to hold the investment for a period of time sufficient to allow for any anticipated recovery in market value. At June 30, 2019, there were no securities in unrealized loss positions.

6. Balance Sheet Details

Prepaid expenses and other current assets consisted of the following (in thousands):

	June 30, 2019	December 31, 2018
Prepaid manufacturing and process development costs	$ 2,446	$ 175
Prepaid insurance	616	1,171
Interest receivable	298	265
Prepaid clinical trial costs	82	—
Other prepaids and current assets (including related party amounts of $0 and $28, respectively)	112	77
	$ 3,554	$ 1,688

Property and equipment for the consisted of the following (in thousands):

	June 30, 2019	December 31, 2018
Laboratory equipment	$ 1,797	$ 1,635
Leasehold improvements	126	72
Computer equipment and software	63	—
Furniture and fixtures	55	36
Construction in progress	183	41
	2,224	1,784
Less accumulated depreciation and amortization	(596)	(402)
	$ 1,628	$ 1,382

Accrued liabilities consisted of the following (in thousands):

	June 30, 2019	December 31, 2018
Accrued research and development (including related party amounts of $233 and $59, respectively)	$ 3,268	$ 1,579
Accrued compensation	1,040	895
Stock repurchase liability	961	1,143
Other accrued liabilities (including related party amounts of $41 and $64, respectively)	853	1,197
	$ 6,122	$ 4,814

7. Related Party Transactions

In February 2015, as amended in October 2017, the Company entered into a Support Services Agreement with COI Pharmaceuticals, Inc. ("COI") that outlines the terms of services provided by COI to the Company, as well as the fees charged for such services. Jay Lichter, Ph.D., a member of the Company's board of directors, and Tighe Reardon, the Company's Acting Chief Financial Officer, are each an executive officer and director of COI, a shared service company that provides certain back-office and administrative and research and development support services, including facilities support, to the portfolio companies of Avalon Ventures, a stockholder of the Company. The Company pays COI quarterly prepayments for estimated costs to be incurred under the agreement in such quarter. Either party may terminate the support services agreement by giving 30 days' prior notice. The support services agreement automatically renews in October of each year unless terminated by either party by giving 30 days' prior notice.

Expense recognized by the Company under the support services agreement with COI and costs incurred pursuant to a sublease with COI, as further described in Note 8, for the periods presented were as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Research and development	$ 167	$ 136	$ 319	$ 312
General and administrative	75	69	154	132
	$ 242	$ 205	$ 473	$ 444

At June 30, 2019 and December 31, 2018, the Company had accounts payable and accrued expenses due to COI of $0.1 million and $0.1 million, respectively. As of December 31, 2018 the Company had prepaid expenses to COI of less than $0.1 million. No amounts were due from COI and the Company had no prepaid expenses to COI at June 30, 2019.

Research Funding and Option Agreement

In July 2014, the Company entered into a Research Funding and Option Agreement (the "Research Agreement") for certain technologies from The Scripps Research Institute ("TSRI") where a member of the Company's board of directors was formerly a faculty member. Pursuant to the agreement, as last amended July 2019, the Company provides funding to TSRI to conduct certain research activities under a research program. The agreement, as amended, expires in July 2022 or upon the completion of the research program, unless extended by mutual agreement. Under the Research Agreement, TSRI granted the Company an option to enter into a license agreement for certain patent rights and technology related to the research program. As described below, the license agreement was entered into in July 2014, and any intellectual property to which the Company exercises the foregoing option will be included in such license agreement. The Company is obligated to provide future research funding to TSRI pursuant to the Research Agreement, as amended, in the amount of $0.2 million for the remainder of 2019, $0.3 million for 2020 and $0.1 million for 2021.

License Agreement

In July 2014, the Company entered into a License Agreement (the "TSRI License") with TSRI. Under the TSRI License (as amended), TSRI granted the Company an exclusive, worldwide, royalty-bearing, sublicensable, license to certain TSRI patent rights, know-how and biological materials (the "Licensed Technology"), to make, use, sell, offer for sale, and import products covered by the claims of the licensed patent rights or developed by the Company through the use of the Licensed Technology (the "Licensed Products") and to otherwise exploit the Licensed Technology. The Licensed Technology forms the basis for the Company's

proprietary Expanded Genetic Alphabet platform technology. The license granted to the Company by TSRI under the Licensed Technology is subject to certain U.S. Government rights and certain other limited rights retained by TSRI.

In consideration for the license, the Company issued TSRI 30,663 shares of the Company's common stock. In July 2015, the Company issued an additional 8,711 shares of its common stock to TSRI. Beginning in July 2017, and annually thereafter, the Company is required to pay TSRI an immaterial annual minimum royalty. The Company is also obligated to pay running royalties in the low single digit percentages on its or its sublicensees' net sales of the Licensed Products on a country-by-country and product-by-product basis. Certain of these payment obligations may be increased during the pendency of any challenge of the licensed patent rights by the Company, its affiliates, or sublicensees. In the event that the Company is required to obtain a license under patent rights held by a third party to prevent infringement of the Licensed Products, the Company may offset its royalty obligations to TSRI by up to a maximum mid-double digit percentage of any royalties the Company pays to such third party. However, in no event, can the Company reduce the royalties payable to TSRI by more than a mid-double digit percentage in any calendar quarter. The Company's royalty obligations as to each product terminate on a country-by-country basis upon the expiration of the last-to-expire of the licensed patent claims that cover the Licensed Products.

In addition, the Company is also required to pay TSRI (i) an amount in the low-double digit percent range of sublicensing revenues, (ii) an amount in the high-single digit percent range of non-sublicensing transaction revenues, such as amounts received for grants of licenses to third parties and grants of other distribution or marketing rights, payable in shares of the Company's capital stock and (iii) milestone payments of up to $2.4 million for each Licensed Product. In June 2019, the Company incurred a milestone obligation of $0.1 million related to the initiation of its Phase 1/2 clinical trial for its lead product candidate, THOR-707.

The Company is responsible for reimbursing TSRI for its patent costs incurred in connection with prosecuting and maintaining the TSRI License patent rights. The parties may terminate the TSRI License at any time by mutual agreement. In addition, the Company may terminate the TSRI License by giving 90 days' notice to TSRI and TSRI may terminate the TSRI License immediately in the event of certain breaches of the agreement by the Company or upon the Company's failure to undertake certain activities in furtherance of commercial development goals. Unless terminated earlier by either or both parties, the term of the TSRI License will continue until the final expiration of all royalty obligations under the agreement.

Academic Development Program Awards

The Company has incurred research and development expense in connection with academic development program awards to TSRI to fund direct research. A member of the Company's board of directors was formerly a faculty member at TSRI and such payments were used to fund a portion of his research activities conducted at TSRI.

Expense recognized by the Company related to the above agreements with TSRI for the periods presented was as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Research and development	$ 191	$ 93	$ 279	$ 187
General and administrative	1	2	4	4
	$ 192	$ 95	$ 283	$ 191

As of June 30, 2019 and December 31, 2018, the Company had accounts payable and accrued expenses due to TSRI of $0.2 million and $0.1 million, respectively. The Company had no prepaid expenses to TSRI as of June 30, 2019 and December 31, 2018, respectively.

8. Commitments and Contingencies

Operating Lease

In August 2017, the Company entered into a sublease with COI, a related party, for its corporate office and laboratory space in La Jolla, California (the "2017 Sublease"). In November 2018, the Company amended the 2017 Sublease to provide the Company with a one-time right to terminate as of March 1, 2024, subject to certain conditions and fees. The 2017 Sublease, as amended, which expires in February 2027, contains rent escalations and the Company is required to pay for common area maintenance and other costs during the term of the lease. In connection with the 2017 Sublease, the Company recognized an operating lease right-of-use asset of

$2.0 million as of June 30, 2019 and an aggregate lease liability of $2.1 million in its balance sheet. The remaining lease term is 7 years and 8 months, and the estimated incremental borrowing rate used by the Company to recognize the lease liability was 8.5%. The right to early terminate the lease was not recognized as part of the Company's lease liability and right-of-use lease asset.

In addition, in September 2018, the Company entered into a noncancelable operating lease for additional corporate office and laboratory space (the "Lease"). The Lease commenced in November 2018 and will expire in February 2023, however, the Company has the option to extend the Lease for a 12-month period. The Lease provided for abatement of rent during the first four months of the lease, contains rent escalations and the Company is required to pay for common area maintenance and other costs during the term of the lease. In connection with the Lease, the Company recognized an operating lease right-of-use asset of $1.0 million as of June 30, 2019 and an aggregate lease liability of $1.1 million in its balance sheet. The remaining lease term is 3 years and 9 months, and the estimated incremental borrowing rate used by the Company to recognize the lease liability was 7%. The option to extend the lease was not recognized as part of the Company's lease liability and right-of-use lease asset.

Future minimum lease payments under the 2017 Sublease and the Lease as of June 30, 2019 are as follows (in thousands):

2019	$ 335
2020	655
2021	675
2022	727
2023	483
Thereafter	1,327
Total future minimum lease payments	4,202
Less interest	(981)
Total lease liability	$ 3,221
Weighted average lease term	6.5 years
Weighted average discount rate	8.1%

Operating lease costs were $0.3 million and $0.6 million for the three and six months ended June 30, 2019, respectively. Operating lease costs were $0.2 million and $0.1 million for the three and six months ended June 30, 2018, respectively.

Contingencies

From time to time, the Company becomes subject to claims or suits arising in the ordinary course of business. The Company accrues a liability for such matters when it is probable that future expenditures will be made and such expenditures can be reasonably estimated. The Company had no such contingent liabilities as of June 30, 2019 or December 31, 2018, respectively.

9. Convertible Preferred Stock and Stockholders' Equity (Deficit)

Authorized Shares

In connection with the completion of the Company's initial public offering ("IPO") in December 2018, the Company amended its Certificate of Incorporation to authorize 200,000,000 shares of common stock, par value $0.001 per share, and 10,000,000 shares of preferred stock, par value $0.001 per share, respectively.

Public Offering and Related Transaction

In December 2018, the Company completed its IPO selling 13,699,636 shares its common stock at $11.00 per share. Proceeds from the Company's IPO, net of underwriting discounts and commissions and other offering costs, were $137.5 million. In connection with the IPO, all 26,737,354 shares of convertible preferred stock outstanding at the time of the IPO converted into 16,687,477 shares of the Company's common stock.

Convertible Preferred Stock

Prior to its conversion to common stock, the Company's convertible preferred stock was classified as temporary equity on the Company's balance sheets in accordance with authoritative guidance for the classification and measurement of potentially redeemable

securities whose redemption is based upon certain change in control events outside of the Company's control, including liquidation, sale or transfer of control of the Company. The Company had determined not to adjust the carrying values of the convertible preferred stock to the liquidation preferences of such shares because of the uncertainty of whether or when such events would occur.

During the year ended December 31, 2018, the Company issued convertible preferred stock as follows:

- in April 2018, the Company issued 8,118,108 shares of Series C convertible preferred stock, raising proceeds, net of offering costs, of $26.3 million; and
- in November 2018, the Company issued 11,365,348 shares of Series C convertible preferred stock, raising proceeds, net of offering costs, of $37.1 million.

Equity Incentive Plans

In November 2018, the Company's board of directors and stockholders approved the 2018 Plan that became effective upon the date of the underwriting agreement related to the IPO. Upon adoption of the 2018 Plan, the Company restricted future grants from its 2014 Plan. A total of 3,428,492 new shares of common stock were initially reserved for issuance under the 2018 Plan. The number of shares reserved under the 2018 Plan also include 87,111 shares of common stock that remained available for issuance under the 2014 Plan at the time the 2018 Plan became effective, and will be increased by the number of shares under the 2014 Plan that are repurchased, forfeited, expired or cancelled on or after the effective date of the 2018 Plan. In addition, the number of shares of common stock available for issuance under the 2018 Plan will automatically increase on January 1 of each calendar year, starting on January 1, 2019 through January 1, 2028, in an amount equal to 4% of the total number of shares of the Company's common stock on the last day of the calendar month before the date of each automatic increase, or a lesser number of shares determined by the Company's board of directors. On January 1, 2019, 1,284,158 shares were automatically added to the 2018 Plan pursuant to the provision.

Early Exercise of Stock Options

Certain stock options granted under the Company's 2014 Plan provide option holders the right to elect to exercise unvested options in exchange for restricted common stock. A summary of the early exercised shares is as follows:

	Shares
Balance as of December 31, 2018	709,123
Shares vested	(156,490)
Balance as of June 30, 2019	552,633

The shares are subject to repurchase by the Company at the original exercise price in the event the optionee's service is terminated either voluntarily or involuntarily prior to vesting. As of June 30, 2019 and December 31, 2018, the Company recorded accrued liabilities of $1.0 million and $1.1 million, respectively, associated with the repurchase rights for early exercised stock options.

2018 Employee Stock Purchase Plan

In November 2018, the Company's board of directors and stockholders approved and adopted the ESPP that became effective immediately prior to the date of the underwriting agreement related to the IPO. The ESPP permits eligible employees who elect to participate in an offering under the ESPP to have up to 15% of their eligible earnings withheld, subject to certain limitations, to purchase shares of common stock pursuant to the ESPP. The price of common stock purchased under the ESPP is equal to 85 percent of the lower of the fair market value of the common stock at the commencement date of each offering period or the relevant date of purchase. A total of 645,000 shares of common stock were initially reserved for issuance under the ESPP. In addition, the number of shares of common stock available for issuance under the ESPP will automatically increase on January 1 of each calendar year, starting on January 1, 2019 through January 1, 2028, in an amount equal to the lesser of (i) 1% of the total number of shares of the Company's common stock on the last day of the calendar month before the date of each automatic increase and (ii) 750,000 shares; provided that before the date of any such increase, the Company's board of directors may determine that such increase will be less than the amount set forth in clauses (i) and (ii). On January 1, 2019, 321,039 shares were automatically added to the ESPP pursuant to the provision.

As of June 30, 2019, 26,430 shares had been issued under the ESPP.

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

You should read the following discussion and analysis together with our unaudited financial statements and notes thereto included in "Item 1. Financial Statements" of this Quarterly Report on Form 10-Q and the audited financial statements and notes thereto as of and for the year ended December 31, 2018 included in the Annual Report on Form 10-K, filed with the Securities and Exchange Commission, or the SEC, on March 12, 2019. In addition to historical information, this Quarterly Report contains forward-looking statements that involve risks, uncertainties, and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors, including but not limited to those set forth under the caption "Risk Factors" in the Annual Report, and the caption "Risk Factors" in this Quarterly Report, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Furthermore, past operating results are not necessarily indicative of results that may occur in future periods.

Overview

We are a clinical-stage biopharmaceutical company focused on prolonging and improving the lives of people with cancer and autoimmune disorders. Our proprietary, first-of-its kind platform technology expands the genetic code by adding a new DNA base pair and is designed to create optimized biologics, which we refer to as Synthorins. A Synthorin is a protein optimized through incorporation of novel amino acids encoded by our new DNA base pair that enables site-specific modifications, which enhance the pharmacological properties of these therapeutics. Our lead product candidate, THOR-707, is a variant of IL-2 designed to kill tumor cells by increasing CD8+ T and NK cells without causing vascular leak syndrome observed with approved recombinant IL-2 (aldesleukin). Based on our preclinical studies, we believe our platform technology can generate a pipeline of additional therapeutics that are more effective, better tolerated or have enhanced ease of use when compared to drugs that have been engineered by other means. We have worldwide rights to our Expanded Genetic Alphabet platform technology and our Synthorins.

We are initially using our Expanded Genetic Alphabet platform technology to develop cytokine Synthorins that target validated mechanisms of action with large market opportunities, in which existing therapies have significant drawbacks. We have designed cytokine Synthorin programs, including IL-2, IL-10 and IL-15, for the treatment of cancer, and another IL-2 Synthorin program for the treatment of autoimmune disorders. We plan to develop THOR-707 to treat multiple tumor types. In the second quarter of 2019, we filed an investigational new drug, or IND, application with the Food and Drug Association, or FDA, and initiated a Phase 1/2 dose escalation and expansion clinical trial of THOR-707. The study in multiple solid tumor types, is examining safety and tolerability, pharmacokinetics, pharmacodynamics and anti-tumor effects of THOR-707 as both a single agent and in combination with an immune checkpoint inhibitor. We plan to specify particular indications for THOR-707 after our initial clinical trials. In our studies of THOR-707 we plan to target indications historically sensitive to IL-2 and PD-1 inhibitors, such as melanoma, renal cell carcinoma, non-small cell lung cancer and urothelial cancer. Our second development program is focused on the development of an IL-2 Synthorin for autoimmune indications, initially in diseases such as chronic graft versus host disease, or GVHD, atopic dermatitis and Crohn's disease. We have several lead IL-2 AI Synthorin molecules that have demonstrated activity in *in vivo* studies. We intend to nominate a lead IL-2 AI Synthorin product candidate in 2019 and start IND-enabling studies thereafter. We plan to file an IND in 2020 for the IL-2 AI product candidate and begin clinical development thereafter. We began *in vitro* and *ex vivo* studies of our Synthorin IL-10 in the first half of 2019 and expect to select a clinical candidate in the second half of the year. We have also identified multiple IL-15 Synthorins and have begun *ex vivo* and *in vivo* evaluation.

To date, we have incurred significant net losses since our inception and as of June 30, 2019 had an accumulated deficit of $92.7 million. Our net losses have resulted primarily from costs incurred in connection with raising capital, research and development activities and general and administrative expenses. We also incurred a $36.0 million non-cash charge in 2018 from the increase in the fair value of a convertible preferred stock purchase right granted in April 2018 and settled in November 2018. We do not have any products approved for sale and have not generated any revenue from product sales or otherwise.

We expect to incur operating losses for the foreseeable future as we pursue the clinical and preclinical development of our programs. Furthermore, we anticipate these losses will increase substantially as we continue our research and development of, and eventually seek regulatory approvals for, our lead product candidate, THOR-707, and any other future product candidates, and as we expand our clinical, regulatory, quality and manufacturing capabilities, incur significant commercialization expenses for marketing, sales, manufacturing and distribution, if we obtain marketing approval for any of our product candidates, and incur additional costs associated with operating as a public company. Accordingly, until such time as we can generate significant revenue from sales of our product candidates, if ever, we expect to finance our cash needs through public or private equity offerings, debt financings, collaborations and licensing arrangements or other capital sources.

In December 2018, we completed our initial public offering in which we sold 13,699,636 million shares of our common stock at $11.00 per share and received net proceeds, after underwriting discount and offering costs, of $137.5 million. Further, in April and November 2018, we issued a total of 19,483,456 shares of Series C convertible preferred stock at a price of $3.2699 per share, resulting in aggregate proceeds, net of offering costs, of $63.4 million. Upon the closing of our initial public offering, all 26,737,354 outstanding shares of our convertible preferred stock automatically converted into 16,687,477shares of common stock.

Financial Operations Overview

Research and Development Expenses

To date, our research and development expenses have related primarily to development of our Expanded Genetic Alphabet platform technology and discovery efforts, preclinical studies and other preclinical activities related to our portfolio of Synthorins, including our lead product candidate, THOR-707. Further, in the second quarter of 2019, we initiated a Phase 1/2 clinical trial for THOR-707 and have begun incurring clinical trial costs. Research and development expenses are recognized as incurred and payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received.

Research and development expenses include:

- external research and development expenses incurred under agreements with contract research organizations, or CROs, investigative sites and consultants to conduct our clinical trials and preclinical and non-clinical studies;
- costs related to manufacturing THOR-707 and our other product candidates for clinical and preclinical studies, including fees paid to third-party manufacturers and raw material suppliers;
- laboratory supplies;
- salaries, payroll taxes, employee benefits, and stock-based compensation charges for those individuals involved in research and development efforts;
- license fees and research funding to TSRI; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent, maintenance of facilities, insurance, equipment and other supplies.

Our direct research and development expenses consist principally of external costs, such as fees paid to CROs, investigative sites and consultants in connection with our clinical trials and preclinical and non-clinical studies, and costs related to manufacturing materials for these studies. Prior to our identification of potential product candidates in our IL-2 IO program in late 2017, we did not track external costs by program. Subsequent to the identification of potential product candidates, a significant majority of our direct research and development costs are related to these IL-2 IO Synthorins and, more specifically, THOR-707. We deploy our personnel and facility related resources across all of our research and development activities.

We plan to substantially increase our research and development expenses for the foreseeable future as we continue the development of THOR-707 and the discovery and development of new product candidates. We cannot determine with certainty the timing of initiation, the duration or the completion costs of future clinical trials and preclinical studies of product candidates due to the inherently unpredictable nature of clinical and preclinical development. Clinical and preclinical development timelines, the probability of success and development costs can differ materially from expectations. We anticipate that we will make determinations as to which product candidates and development programs to pursue and how much funding to direct to each product candidate or program on an ongoing basis in response to the results of ongoing and future clinical trials and preclinical studies, regulatory developments and our ongoing assessments as to each product candidate's commercial potential.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and employee-related costs, including stock-based compensation, for personnel in executive, finance and other administrative functions. Other significant costs include legal fees relating to intellectual property and corporate matters, professional fees for accounting and consulting services, insurance costs and facility-related costs. We anticipate that our general and administrative expenses will increase in the future to support our continued research and development activities and, if any product candidates receive marketing approval, commercialization activities. We also anticipate increased expenses related to audit, legal, regulatory, and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums, and investor relations costs associated with operating as a public company.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our condensed financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of these condensed financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments used in our accounting practices and reflect the effects of revisions in the period in which they are deemed necessary. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our critical accounting policies are those accounting principles generally accepted in the United States that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations, as well as the specific manner in which we apply those principles. For a description of our critical accounting policies, please see Management's Discussion and Analysis of Financial Condition and Results of Operations included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018. There have not been any material changes to our critical accounting policies since December 31, 2018.

Results of Operations

Comparison of the Three Months Ended June 30, 2019 and 2018

The following table summarizes our results of operations for the three months ended June 30, 2019 and 2018:

	Three Months Ended June 30,		
(in thousands)	**2019**	**2018**	**Change**
Operating expenses:			
Research and development	$ 10,425	$ 3,387	$ 7,038
General and administrative	3,040	602	2,438
Total operating expenses	13,465	3,989	9,476
Loss from operations	(13,465)	(3,989)	(9,476)
Change in fair value of preferred stock purchase right liability	—	(14)	14
Interest Income	1,095	—	1,095
Net loss	$ (12,370)	$ (4,003)	$ (8,367)

Research and Development Expenses. Research and development expenses were $10.4 million and $3.4 million for the three months ended June 30, 2019 and 2018, respectively. The increase of $7.0 million was due primarily to an increase in external expense related to our THOR-707 program and increased personnel and related expenses, as we have increased our research and development headcount to support our development programs. We also incurred additional external costs on our other development programs during the six months ended June 30, 2019 as compared to same period in 2018, including our IL-2 AI program.

General and Administrative Expenses. General and administrative expenses for the three months ended June 30, 2019 were $3.0 million and $0.6 million incurred for the same period in 2018. The increase of $2.4 million in expenses in 2019 was due primarily to increased personnel and related expenses, including $0.6 million of additional non-cash stock-based compensation expense, as we have increased our general and administrative headcount to support our expanding operations. Furthermore, we incurred additional costs during the three months ended June 30, 2019 that were not incurred in during the same period in 2018 as we now operate as a public company, including additional insurance, legal and accounting fees.

Interest Income. The $1.1 million of interest income recognized for the three months ended June 30, 2019 was primarily due to an increase in our excess cash reserves, primarily from our initial public offering in December 2018, and the execution of our investment policy in the fourth quarter of 2018 whereby we began investing our excess cash reserves in investment securities and interest-bearing money-market accounts. Prior to the fourth quarter of 2018, our excess cash reserves were in a non-interest-bearing account and hence there was no similar income for the three months ended June 30, 2018.

Comparison of the Six Months Ended June 30, 2019 and 2018

The following table summarizes our results of operations for the six months ended June 30, 2019 and 2018:

(in thousands)	Six Months Ended June 30, 2019	2018	Change
Operating expenses:			
Research and development	$ 19,989	$ 5,152	$ 14,837
General and administrative	5,395	1,027	4,368
Total operating expenses	25,384	6,179	19,205
Loss from operations	(25,384)	(6,179)	(19,205)
Change in fair value of preferred stock purchase right liability	—	(14)	14
Interest Income	2,163	—	2,163
	$ (23,221)	$ (6,193)	$ (17,028)

Research and Development Expenses. Research and development expenses were $20.0 million and $5.2 million for the six months ended June 30, 2019 and 2018, respectively. The increase of $14.8 million was due primarily to an increase in external expense related to our THOR-707 program and an increase in personnel and related expenses as we have increased our research and development headcount to support our development programs, including $0.4 million of additional non-cash stock-based compensation expense. We also incurred additional external costs on our other development programs during the six months ended June 30, 2019 as compared to same period in 2018, including our IL-2 AI program.

General and Administrative Expenses. General and administrative expenses for the six months ended June 30, 2019 were $5.4 million, an increase of $4.4 million from the $1.0 million incurred for the same period in 2018. The increase in expenses over the six-month period in 2019 was due primarily to increased personnel and related expenses, including $0.8 million of additional non-cash stock-based compensation expense, as we have increased our general and administrative headcount to support our expanding operations. Furthermore, we incurred additional costs during the six months ended June 30, 2019 related to patent application filings as compared to 2018, and are incurring costs in 2019 that were not incurred in during the same period in 2018 as we now operate as a public company, including additional insurance, legal and accounting fees.

Interest Income. The $2.2 million of interest income recognized for the six months ended June 30, 2019 was primarily due to an increase in our excess cash reserves, primarily from our initial public offering in December 2018, and the execution of our investment policy in the fourth quarter of 2018 whereby we began investing our excess cash reserves in investment securities and interest-bearing money-market accounts. Prior to the fourth quarter of 2018, our excess cash reserves were in a non-interest-bearing account and hence there was no similar income for the six months ended June 30, 2018.

Liquidity and Capital Resources

We have incurred net losses and negative cash flows from operations since our inception and anticipate we will continue to incur net losses for the foreseeable future. Since inception, we have financed our operations primarily through the sale of our equity securities and we will need to raise substantial additional capital in the future. For example, in 2018, we raised proceeds, net of offering costs, of $137.5 million from our initial public offering in December 2018, and $63.4 million from the sale of our Series C convertible preferred stock in April and November 2018.

As of June 30, 2019 we had $23.5 million of cash and cash equivalents, a decrease of $164.8 million from the $188.4 million of cash and cash equivalents at December 31, 2018. The decrease in our cash and cash equivalents balance during the six months ended June 30, 2019 was primarily due to the execution of our investment policy during the period whereby we began investing a significant portion of our excess cash reserves in available-for-sale investment securities. Further detail of the change in our cash and cash equivalents for the six months ended June 30, 2019 and 2018 is summarized below.

(in thousands)	Six Months Ended June 30, 2019	2018
Net cash (used in) provided by:		
Operating activities	$ (24,531)	$ (5,267)
Investing activities	(140,636)	(337)
Financing activities	345	26,256
Net (decrease) increase in cash and cash equivalents	$ (164,822)	$ 20,652

Operating Activities

Net cash used in operating activities was $24.5 million for the six months ended June 30, 2019, as compared to $5.3 million for same period in 2018. The $19.3 million increase in net cash used in operating activities was primarily due to an increase of $17.0 million in our net loss for the 2019 period as compared to the 2018 period. This increase in our net loss was mostly due to the advancement of our research and development programs, including THOR-707, and increased personnel costs to support these activities and our operations as a public company. Further, additional prepayments were made during the six months ended June 30, 2019, as compared to the same period in 2018, to support our program development initiatives.

Investing Activities

Net cash used in investing activities for the six months ended June 30, 2019 was primarily due to the execution of our investment policy whereby we began investing our excess cash reserves, including the $137.5 million of net proceeds from our initial public offering in December 2018, in investment securities in accordance with our investment policy. In addition, we purchased property and equipment in each period, primarily consisting of laboratory equipment.

Financing Activities and Funding Requirements

Net cash provided by financing activities for the six months ended June 30, 2018, was primarily due to the net proceeds from the issuance of our first tranche of Series C convertible preferred stock in April 2018. The cash provided by financing activities for the six months ended June 30, 2019, was from stock purchases pursuant to our employee stock purchase plan and the exercise of stock options that occurred during the period.

We believe that our existing cash and cash equivalent balance will be sufficient to meet our anticipated cash requirements through at least the next 12 months. However, 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. We have based this estimate on assumptions that may prove to be wrong, and we could deplete our capital resources sooner than we expect. Additionally, the process of testing product candidates in clinical trials is costly, and the timing of progress and expenses in these trials is uncertain.

Our future capital requirements will depend on many factors, including:

- the progress, timing, costs and results of our ongoing Phase 1/2 clinical trial of THOR-707;
- the initiation, progress, timing, costs and results of drug discovery, preclinical studies and clinical trials of our other future product candidates;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- the cost of manufacturing THOR-707 and future product candidates for clinical trials in preparation for marketing approval and in preparation for commercialization;
- the costs of any third-party products used in our combination clinical trials that are not covered by such third party or other sources;
- the costs associated with hiring additional personnel and consultants as our clinical and preclinical activities increase;
- the receipt of marketing approval and revenue received from any potential commercial sales of THOR-707 or other product candidates;
- the cost of commercialization activities for THOR-707 and future product candidates we develop if we receive marketing approval, including marketing, sales and distribution costs;
- the emergence of competing therapies and other adverse market developments;
- the ability to establish and maintain strategic licensing or other arrangements and the financial terms of such agreements;
- the amount and timing of any payments we may be required to make pursuant to the TSRI Agreement, or other future license agreements;
- the costs involved in preparing, filing, prosecuting, maintaining, expanding, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the extent to which we in-license or acquire other products and technologies; and

- the costs of operating as a public company.

Until we are able to generate sufficient cash from our operations, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations and licensing arrangements or other sources. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations, or other similar arrangements with third parties, we may have to relinquish valuable rights to our platform technology, future revenue streams, research programs or product candidates or may have to grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. If we are unable to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and could force us to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates or to our platform technology that we would otherwise prefer to develop and market ourselves.

Off-Balance Sheet Arrangements

During the periods presented we did not have, nor do we currently have, any off-balance sheet arrangements as defined by applicable regulations of the SEC.

Recent Accounting Pronouncements

See Item 1 of Part I, "Notes to Condensed Consolidated Financial Statements — Note 2 — Basis of Presentation and Summary of Significant Accounting Policies" for a discussion of recent accounting pronouncements.

ITEM 3. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Risk

The primary objective of our investment activities is to preserve principal and liquidity while at the same time maximizing the income we receive without significantly increasing risk. To achieve this objective, we invest in money market funds, U.S. Treasury notes, and high-quality marketable debt instruments of corporations and government sponsored enterprises with contractual maturity dates of generally less than two years, in accordance with an investment policy approved by our audit committee. Some of the financial instruments that we invest in could be subject to market risk, meaning that a change in prevailing interest rates may cause the value of the instruments to fluctuate. For example, if we purchase a security that was issued with a fixed interest rate and the prevailing interest rate later rises, the value of that security will probably decline. To minimize this risk, we intend to maintain a portfolio which may include a variety of securities, including money market funds, government debt securities and commercial paper, all with various maturity dates.

Based on our current investment portfolio, we do not believe that our results of operations would be materially impacted by an immediate change of 10% in interest rates.

ITEM 4. Controls and Procedures.

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Acting Chief Financial Officer (our principal executive officer and principal financial officer, respectively), as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

As of June 30, 2019, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Acting Chief Financial Officer, of the effectiveness of the design and operation of 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. Based on this evaluation, our Chief Executive Officer and Acting Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of June 30, 2019.

An evaluation was also performed under the supervision and with the participation of our management, including our Chief Executive Officer and Acting Chief Financial Officer, of any change in our internal control over financial reporting that occurred during our last fiscal quarter and that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. That evaluation did not identify any changes in our internal control over financial reporting that occurred during our latest fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

ITEM 1. Legal Proceedings.

From time to time, we may become involved in litigation or other legal proceedings. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

ITEM 1A. Risk Factors.

We operate in a dynamic and rapidly changing environment that involves numerous risks and uncertainties. Certain factors may have a material adverse effect on our business, financial condition and results of operations, and you should carefully consider them. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risks described below, together with the other information contained in this Quarterly Report and in our other public filings. The risk factors set forth below that are marked with an asterisk (*) did not appear as separate risk factors in, or contain changes to the similarly titled risk factor included in Item 1A. of our Annual Report on Form 10-K, filed with the SEC on March 12, 2019. If any of the following risks actually occur, our business, financial condition, results of operations, and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our results of operations and financial condition.

Risks Related to Our Business and Industry

We have a limited operating history, have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future. We may never generate any revenue or become profitable or, if we achieve profitability, we may not be able to sustain it.*

We are an early stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We commenced operations in 2014. To date, we have focused primarily on organizing and staffing our company, business planning, raising capital, in-licensing our platform technology, optimizing the licensed technology, identifying potential product candidates, enhancing our intellectual property portfolio and undertaking research and preclinical studies and enabling manufacturing for our development programs. Our approach to the discovery and development of product candidates based on our Expanded Genetic Alphabet platform technology is unproven, and we do not know whether we will be able to develop any products of commercial value. In addition, we currently only have one product candidate, THOR-707, which recently commenced clinical development, and all our other development programs are in the discovery or preclinical stages. We have only limited experience filing an IND and manufacturing a clinical scale product candidate, and we have not yet demonstrated an ability to successfully complete any Phase 1, Phase 2 or pivotal clinical trials, obtain regulatory approvals, continue to manufacture product for clinical studies or to manufacture product at a commercial scale, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing biopharmaceutical products.

We have incurred significant operating losses since our inception and have not yet generated any revenue. If our products are not successfully developed and approved, we may never generate any revenue. For example, our net loss was $56.6 million, $5.9 million and $3.1 million for the years ended December 31, 2018, 2017 and 2016, respectively and as of June 30, 2019 we had an accumulated deficit of $92.7 million. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase substantially as THOR-707 and any future product candidates advance through preclinical studies and clinical trials, and as we expand our clinical, regulatory, quality and manufacturing capabilities, incur significant commercialization expenses for marketing, sales, manufacturing and distribution, if we obtain marketing approval for any of our product candidates, and incur additional costs associated with operating as a public company. The net losses we incur may fluctuate significantly from quarter to quarter.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able 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 depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product candidates or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

If we are unable to raise additional capital when needed, we may be forced to delay, reduce or eliminate our development programs or other operations.*

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. We expect to continue to incur significant expenses and operating losses over the next several years as we pursue development of research programs and marketing approvals for our IL-2 Synthorins for the treatment of cancer and autoimmune disorders and advance any other product candidates that we may develop or otherwise acquire. In addition, our product candidates, if approved, may not achieve commercial success. Our revenue, if any, will be derived from sales of products that we do not expect to be commercially available for several years, if at all. If we obtain marketing approval for THOR-707 or any other product candidates that we develop, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Some of these expenses may be incurred in advance of marketing approval and could be substantial. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to develop and commercialize our current and any future drug candidates, and otherwise pursue our business strategy. We also expect an increase in our expenses associated with creating additional infrastructure to support operations as a public reporting company.

As of June 30, 2019, we had cash, cash equivalents and investment securities of $165.2 million. We believe that our existing cash, cash equivalents and investment securities, will enable us to fund our operating expenses and capital expenditure requirements through at least the next 12 months. In particular, we expect that our existing cash, cash equivalents and investment securities will allow us to report clinical biomarker proof-of-concept data for THOR-707 as a single agent and in combination with an immune checkpoint inhibitor, identify a product candidate in the IL-2 AI Synthorin program and complete IND-enabling studies for such program, and identify development candidates for our IL-10 and IL-15 Synthorin programs. Our cash forecasts are based on assumptions that may prove to be wrong, and we could use our available capital resources earlier than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the progress, timing, costs and results of our ongoing Phase 1/2 clinical trial of THOR-707;
- the initiation, progress, timing, costs and results of drug discovery, preclinical studies and clinical trials of our other future product candidates;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- the cost of manufacturing THOR-707 and future product candidates for clinical trials in preparation for marketing approval and in preparation for commercialization;
- the costs of any third-party products used in our combination clinical trials that are not covered by such third party or other sources;
- the costs associated with hiring additional personnel and consultants as our preclinical and clinical activities increase;
- the receipt of marketing approval and revenue received from any potential commercial sales of THOR-707 or other product candidates;
- the cost of commercialization activities for THOR-707 and future product candidates we develop if we receive marketing approval, including marketing, sales and distribution costs;
- the emergence of competing therapies and other adverse market developments;
- the ability to establish and maintain strategic licensing or other arrangements and the financial terms of such agreements;
- the amount and timing of any payments we may be required to make pursuant to our exclusive license agreement with The Scripps Research Institute, as amended, or the TSRI Agreement, or other future license agreements;
- the costs involved in preparing, filing, prosecuting, maintaining, expanding, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the extent to which we in-license or acquire other products and technologies; and
- the costs of operating as a public company.

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

Unless and until we can generate a substantial amount of product revenue, we expect to seek additional capital through a combination of public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Our issuance of additional securities, whether equity or debt, or the possibility of such issuance, may cause the market price of our common stock to decline, and our stockholders may not agree with our financing plans or the terms of such financings. To the extent that we raise additional capital through the sale of equity or convertible debt securities, current stockholders will be diluted and the terms of these securities may include liquidation or other preferences that adversely affect the rights of existing stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to declare dividends, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through collaborations and licensing arrangements with third parties, we may have to relinquish valuable rights to our platform technology or product candidates or grant licenses on terms unfavorable to us. In addition, securing additional financing would require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history. As of December 31, 2018, we had federal and state net operating loss carryforwards of $32.9 million and $32.3 million, respectively. We do not anticipate generating revenue from sales of products for the foreseeable future, if ever, and we may never achieve profitability. Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage points change (by value) in its equity ownership by "5-percent shareholders," as defined in the Code, over a rolling three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. As a result of our prior financings or other transactions, we may have in the past experienced, and we may in the future experience, ownership changes, some of which are outside our control. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards and other pre-change tax attributes to offset U.S. federal taxable income may be subject to limitations, which could result in increased future tax liability to us and could have an adverse effect on our future results of operations. Similar provisions of state tax law may also apply.

Under recently enacted U.S. federal tax legislation, although the treatment of net operating loss carryforwards arising in tax years beginning on or before December 31, 2017 has generally not changed, net operating loss carryforwards arising in tax years beginning after December 31, 2017 may be used to offset only 80% of taxable income and may not be carried back. In addition, net operating losses arising in tax years ending after December 31, 2017 may be carried forward indefinitely, as opposed to the 20-year carryforward under prior law.

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

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

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

Our business is highly dependent on the success of our initial IL-2 Synthorins targeting cancer and autoimmune disorders, which are in the early stages of development. Most of our development programs are in the preclinical or discovery stage and will require significant additional preclinical and clinical development before we can seek regulatory approval for and launch a product commercially.*

Our business and future success is highly dependent on our ability to obtain regulatory approval of and then successfully launch and commercialize our IL-2 Synthorins, including our lead product candidate, THOR-707. We are in the early stages of our development efforts. In the second quarter of 2019, we filed an IND application with the FDA and initiated a Phase 1/2 clinical trial of THOR-707. Most of our other development programs are still in the preclinical or drug discovery stage. We have invested

substantially all of our efforts and financial resources in developing THOR-707 and other potential product candidates and conducting preclinical studies. To date, we have only limited experience filing an IND with the FDA and have only had limited interactions with the FDA regarding our clinical development plans. We plan to file an IND for our IL-2 AI Synthorin lead drug candidate in 2020. THOR-707, as our first planned clinical program, may experience complications surrounding trial execution, patient recruitment and enrollment, other serious adverse events that may result in the FDA putting our trial on clinical hold, or quality and supply of clinical doses.

We are not permitted to market any biological product in the United States until we receive approval of a Biologics License Application, or BLA, from the FDA. We have not previously submitted a BLA to the FDA, or similar marketing application to comparable foreign authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe, pure and potent for each desired indication. A BLA must also include significant information regarding the chemistry, manufacturing and controls for the product, and the manufacturing facilities must complete a successful pre-license inspection.

FDA approval of a BLA is not guaranteed, and the review and approval process is an expensive and uncertain process that may take several years. The FDA also has substantial discretion in the approval process. The number and types of preclinical studies and clinical trials that will be required for BLA approval varies depending on the product candidate, the disease or the condition that the product candidate is designed to treat and the regulations applicable to any particular product candidate. Despite the time and expense associated with preclinical studies and clinical trials, failure can occur at any stage.

The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain approval of any product candidates that we develop based on the completed clinical trials.

Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of THOR-707 and any future product candidates. The success of our product candidates will depend on several factors, including the following:

- completion of preclinical studies and clinical trials with favorable results;
- acceptance of INDs by the FDA or similar regulatory filing by comparable foreign regulatory authorities for the conduct of clinical trials of our product candidates and our proposed design of future clinical trials;
- receipt of marketing approvals from applicable regulatory authorities, including BLAs from the FDA and maintaining such approvals;
- making arrangements with our third-party manufacturers for, or establishing, commercial manufacturing capabilities;
- maintaining an acceptable safety profile of our products following approval; and
- maintaining and growing an organization of scientists and business people who can develop our products and technology.

Generally, public concern regarding the safety of biopharmaceutical products could delay or limit our ability to obtain regulatory approval, result in the inclusion of unfavorable information in our labeling, or require us to undertake other activities that may entail additional costs. We have not obtained FDA approval for any product. This lack of experience may impede our ability to obtain FDA approval in a timely manner, if at all, for THOR-707 or future product candidates.

The success of our business, including our ability to finance our company and generate any revenue in the future, will primarily depend on the successful development, regulatory approval and commercialization of THOR-707, as well as any future product candidates, which may never occur. However, given our early stage of development, it may be several years, if at all, before we have demonstrated the safety and efficacy of a treatment sufficient to warrant approval for commercialization. If we are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize our current or any future product candidates, we may not be able to generate sufficient revenue to continue our business.

Our approach to the discovery and development of product candidates based on our Expanded Genetic Alphabet platform technology is unproven, and we do not know whether we will be able to develop any products of commercial value.*

The success of our business depends primarily upon our ability to discover, develop and commercialize products based on our first-in-kind Expanded Genetic Alphabet platform technology. While we have had favorable preclinical study results related to THOR-707 based on our platform technology and filed an IND with the FDA and initiated a Phase 1/2 clinical trial of THOR-707 in the second quarter of 2019, we have not yet succeeded and may not succeed in demonstrating efficacy and safety for any product candidates in clinical trials or in obtaining marketing approval thereafter. Our approach may be unsuccessful in moving our IL-2 Synthorins from preclinical studies into clinical development, discovering additional product candidates, and any product candidates that we are currently developing may be shown to have harmful side effects or may have other characteristics that may necessitate additional clinical testing or make the product candidates unmarketable or unlikely to receive marketing approval. If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

Preclinical development is uncertain. Our preclinical programs may experience delays or may never advance to clinical trials, which would adversely affect our ability to obtain regulatory approvals or commercialize these programs on a timely basis or at all, which would have an adverse effect on our business.*

Most of our product candidates are still in the preclinical stage, and their risk of failure is high. Before we can commence clinical trials for these product candidates, we must complete extensive preclinical testing and studies that support our planned INDs in the United States, or similar applications in other jurisdictions. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or other regulatory authorities will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of our programs. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin.

Manufacturing Synthorins incorporating our novel amino acids is uncertain and our novel E.coli strain has never produced products at a scale that ensures clinical supply and we have never produced products at a commercial scale. We may be unable to manufacture Synthorins at the scale needed for clinical development, or continued clinical development, and commercial production on a timely basis or at all, which would adversely affect our ability to conduct clinical trials and seek regulatory approvals or commercialize our programs, which would have an adverse effect on our business.*

Although *E.coli* bacteria is commonly used to manufacture therapeutic proteins, we have only limited experience utilizing our novel, proprietary strain to manufacture proteins for clinical trials for any of our product candidates, and it has never been utilized to manufacture proteins for large-scale clinical trials or commercialization of any product candidates. As a result, the risk of delays or failure is high. Before we can commence clinical trials for a product candidate, the Synthorins manufactured using our *E. coli* strain must complete extensive analytical testing and be qualified for use in human studies. We cannot be certain of the timely completion or outcome of our analytical testing and suitability for human studies and cannot predict if the FDA or other regulatory authorities will accept our proposed clinical material or if the outcome of our analytical testing will ultimately support the further development of our programs. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin. In addition, we cannot be certain that we will be able to produce products at the scale required for our clinical trials and, for any approved products, commercial production on a timely basis or at all, which could also have an adverse effect on our business.

Preclinical and clinical trials are expensive, time-consuming and difficult to design and implement, and involve uncertain outcomes. Furthermore, results of earlier preclinical studies and clinical trials may not be predictive of results of future preclinical studies or clinical trials.*

The risk of failure for our current and any future product candidates is high. It is impossible to predict when or if any of our product candidates will complete clinical trials evaluating their safety and effectiveness in humans or will receive regulatory approval. To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe and effective in humans for use in each target indication. To date we only advanced one product candidate into a clinical trial. Preclinical and clinical testing is expensive and can take many years to complete, and the outcome is inherently uncertain. Failure can occur at any time during the preclinical or clinical trial process. The outcome of preclinical testing and early clinical trials may not be predictive of the results of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. In particular, while we are conducting a Phase 1/2 clinical trial of THOR-707, we do not know whether THOR-707 will perform in current or future clinical trials as it has performed in prior preclinical studies. Many companies in the biopharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and we cannot be certain that we will not face similar setbacks. 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. Moreover, preclinical and

clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in clinical trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen and other clinical trial protocols, and the rate of dropout among clinical trial participants. If we fail to produce positive results in our planned preclinical studies or clinical trials of any of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be materially and adversely affected.

We may encounter substantial delays in the commencement or completion, or termination or suspension, of our clinical trials, which could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.*

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidate for its intended indications. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. We may experience numerous unforeseen events during or as a result of clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- we may be unable to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to obtain regulatory authorizations to commence a clinical trial;
- we may experience issues in reaching a consensus with regulatory authorities on trial design;
- regulators or institutional review boards, or IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- changes to a clinical trial protocol;
- clinical trial sites deviating from a trial protocol or dropping out of a trial;
- subjects failing to enroll or remain in clinical trials at the rate we expect, or failing to return for post-treatment follow-up;
- subjects choosing an alternative treatment for the indication for which we are developing our product candidates, or participating in competing clinical trials;
- subjects experiencing severe or unexpected drug-related adverse effects;
- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials, or we may decide to abandon product development programs;
- we may need to add new or additional clinical trial sites;
- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- any changes to manufacturing process that may be necessary or desired;
- the cost of preclinical testing and studies and clinical trials of any product candidates may be greater than we anticipate or greater than our available financial resources; or
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate or we may not be able to obtain sufficient quantities of combination therapies for use in clinical trials.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond the clinical trials and testing that we contemplate, if we are unable to successfully complete clinical trials or other testing of our product candidates, if the results of these clinical trials or tests are unfavorable or are only modestly favorable or if there are safety concerns associated with any of product candidates, we may:

- incur additional unplanned costs;
- be delayed in obtaining marketing approval, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing or other requirements;
- be required to perform additional clinical trials to support approval;
- have regulatory authorities withdraw, or suspend, their approval of the drug or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy, or REMS;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- have the product removed from the market after obtaining marketing approval;
- be subject to lawsuits; or
- experience damage to our reputation.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board for such trial or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

Further, conducting clinical trials in foreign countries, as we may do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

In addition to the factors above, we may make formulation or manufacturing changes to our product candidates, in which case we may need to conduct additional preclinical studies to bridge our modified product candidates to earlier versions, which may be costly, time consuming and may not be successful at all. Our failure to successfully initiate and complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business. We cannot assure you that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our clinical trials. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of our product candidates.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The enrollment of patients depends on many factors, including:

- the severity of the disease under investigation;
- the patient eligibility and the inclusion and exclusion criteria defined in the protocol;
- the size and health of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to study sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the drug candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

In addition, our clinical trials currently compete and will continue to compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial site.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or might require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, slow down or halt our product candidate development and approval process and jeopardize our ability to seek and obtain the marketing approval required to commence product sales and generate revenue, which would cause the value of our company to decline and limit our ability to obtain additional financing if needed. Furthermore, we rely on and expect to continue to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and we will have limited influence over their performance.

Our product candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile 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 to interrupt, delay or halt preclinical studies or could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. As is the case with many treatments for cancer and autoimmune disorders, it is likely that there will be side effects associated with the use of our products. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The treatment-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, our planned clinical trial in combination with an immune checkpoint inhibitor may result in adverse events based on the combination therapy that may negatively impact the reported safety profile in such clinical trial. For example, checkpoint inhibitors have been shown to have adverse events, including immune-related adverse events on the liver and other organ systems, which may limit the maximum dose in our clinical trials or otherwise negatively impact our combination clinical trials.

Further, by design, clinical trials rely on a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. If our product candidates receive marketing approval and we or others identify undesirable side effects caused by such product candidates after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- regulatory authorities may require a REMS plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;
- we may be required to change the way such product candidates are distributed or administered, conduct additional clinical trials or change the labeling of the product candidates;
- we may be subject to regulatory investigations and government enforcement actions;
- regulatory authorities may withdraw or limit their approval of such product candidates;
- we may decide to remove such product candidates from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and
- we may suffer reputational harm.

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

Interim top-line and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim top-line or preliminary data from our clinical studies. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

We expect to develop THOR-707, and potentially future product candidates, in combination with other therapies, and safety or supply issues with combination-use products may delay or prevent development and approval of our product candidates.*

We intend to develop THOR-707, and likely other future product candidates, in combination with one or more cancer therapies, both approved and unapproved. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. Combination therapies are commonly used for the treatment of cancer, and we would be subject to similar risks if we develop any of our product candidates for use in combination with other drugs or for indications other than cancer, such as autoimmune disorders. Similarly, if the therapies we use in combination with our product candidates are replaced as the standard of care for the indications we choose for any of our product candidates, the FDA or similar regulatory authorities outside of the United States may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially.

Our current or planned clinical trials in combination with an immune checkpoint inhibitor may result in adverse events based on the combination therapy that may negatively impact the reported safety profile in such clinical trial. For example, checkpoint inhibitors have been shown to have adverse events, including immune-related adverse events on the liver and other organ systems, which may limit the maximum dose in our clinical trials or otherwise negatively impact our combination clinical trials.

We may not be successful in our efforts to identify or discover additional product candidates.

Although we intend to explore other therapeutic opportunities in addition to the product candidates that we are currently developing, we may fail to identify or discover viable new product candidates for clinical development for a number of reasons. If we fail to identify additional potential product candidates, our business could be materially harmed.

Research programs to pursue the development of our existing and planned product candidates for additional indications and to identify new product candidates and disease targets require substantial technical, financial and human resources whether or not they are ultimately successful. Our research programs may initially show promise in identifying potential indications and/or product candidates, yet fail to yield results for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential indications and/or product candidates;
- potential product candidates may, after further study, be shown to have harmful adverse effects or other characteristics that indicate they are unlikely to be effective drugs; or
- it may take greater human and financial resources than we will possess to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, thereby limiting our ability to develop, diversify and expand our product portfolio.

Accordingly, there can be no assurance that we will ever be able to identify additional therapeutic opportunities for our current product candidate or to develop suitable additional product candidates through internal research programs, which could materially adversely affect our future growth and prospects.

We may become exposed to costly and damaging liability claims and any product liability insurance we may obtain may not cover all damages from such claims.*

We are exposed to potential product liability risks that are inherent in the research, development, manufacturing, marketing and use of biopharmaceutical products. The use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical trials, manufacturing, marketing or sale. 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 or a breach of warranties. Claims could also be asserted under state consumer protection acts.

Although the clinical trial process is designed to identify and assess potential side effects, it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If any of our product candidates were to cause adverse side effects during clinical trials or after approval thereof, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or cease the commercialization of our products. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- delay or termination of clinical trials;
- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant negative financial impact; and
- the inability to commercialize our product candidates.

Although we will seek to procure product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. As the expense of insurance coverage is increasing, we may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be materially harmed.

We have never commercialized a product candidate and we may lack the necessary expertise, personnel and resources to successfully commercialize any of our products that receive regulatory approval on our own or together with collaborators.

We have never commercialized a product candidate. We currently have no sales force, marketing or distribution capabilities. To achieve commercial success of our product candidates, if any are approved, we will have to develop our own sales, marketing and supply capabilities or outsource these activities to one or more third parties.

Factors that may affect our ability to commercialize our product candidates on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, obtaining access to or persuading adequate numbers of physicians to prescribe our product candidates and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization requires significant investment, is time-consuming and could delay the launch of our product candidates. We may not be able to build an effective sales and marketing organization in the United States, the European Union or other key global markets. To the extent we need to rely upon one or more third parties, we may have little or no control over the marketing and sales efforts of those third parties and our revenue from product sales may be lower than if we had commercialized our product candidates ourselves. We will also face competition in any search for third parties to assist us with the sales and marketing efforts of our product candidates. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our product candidates, we may have difficulties generating revenue from them.

The successful commercialization of our product candidates will depend in part on the extent to which we obtain and maintain favorable coverage, adequate reimbursement levels and pricing policies with third party payors.

The availability and adequacy of coverage and reimbursement by third-party payors, including governmental healthcare programs such as Medicare and Medicaid, managed care organizations, and private health insurers, are essential for most patients to be able to afford prescription medications such as our product candidates, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for products by third-party payors will have an effect on our ability to successfully commercialize our product candidates. We cannot be sure that coverage and reimbursement in the United States, the European Union or elsewhere will be available for our product candidates, if approved, or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

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 or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates 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 candidates, pricing of existing third-party therapeutics may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates, if approved. Even if our product candidates are approved and we obtain coverage for our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Interim reimbursement levels for new medicines, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Net prices for medicines may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of medicines from countries where they may be sold at lower prices than in the United States. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, if approved, and may not be able to obtain a satisfactory financial return on our product candidates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly-approved products. The regulations that govern marketing approvals, pricing, and reimbursement for new medicines vary widely from country to country. In the United States, third-party payors play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how third-party payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates, if approved.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor and coverage and reimbursement by one payor does not guarantee coverage and reimbursement by another 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 product candidates 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 on short notice, and we believe that changes in these rules and regulations are likely.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical, specialty pharmaceutical and biotechnology companies among others. We compete in the segments of the pharmaceutical, biotechnology and other related markets that develop immunotherapies for the treatment of cancer as well as drugs targeting autoimmune disorders. There are other companies working to develop immunotherapies for the treatment of cancer and drugs targeting autoimmune disorders including divisions of pharmaceutical and biotechnology companies of various sizes. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

We are developing our initial product candidates for the treatment of cancer and autoimmune disorders and currently none of these therapies are approved. There are already a variety of available drug therapies marketed for cancer and some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic products. This may make it difficult for us to achieve our business strategy of using our product candidates in combination with existing therapies or replacing existing therapies with our product candidates.

Competition may further increase as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. We are aware that Ambrx Inc., Admune Therapeutics (Novartis AG), Alkermes plc, Anaveon AG, Avadel Pharmaceuticals plc, Alopexx Oncology LLC, Altor BioSciences, Inc., Armo BioSciences (Eli Lilly and Company), AstraZeneca plc, Bristol-Myers Squibb, Cue Biopharma, Inc., Cytune Pharma, Medicenna Therapeutics Corp, Nektar Therapeutics, Neoleukin Therapeutics, Inc., Philogen S.p.A., Roche AG, Sutro Biopharma, Inc., Xencor, Inc. and Xoma Corporation are developing IL-2, IL-10 or IL-15 cytokine programs for oncology and Proleukin (aldesleukin) is marketed by Nestle S.A. for the treatment of metastatic RCC and melanoma. Additionally, we are aware that Amgen Inc., Eli Lilly and Company, Delinia, Inc. (Celgene Corporation), ILTOO Pharma (Les Laboratoires Servier SAS), Medicenna, Nektar and Roche have modified or low-dose IL-2 programs in development for the treatment of autoimmune disorders. Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop.

Established pharmaceutical companies may invest heavily to accelerate discovery and development of novel product candidates or to in-license novel product candidates that could make our product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, discovering, developing, receiving FDA approval for or commercializing drugs before we do, which would have an adverse impact on our business and results of operations.

The availability of our competitors' products could limit the demand and the price we are able to charge for any product candidate we commercialize, if any. The inability to compete with existing or subsequently introduced drugs would harm our business, financial condition and results of operations.

We expect the product candidates we develop will be regulated as biological products, or biologics, and therefore they may be subject to competition sooner than anticipated.

The Biologics Price Competition and Innovation Act of 2009 (BPCIA) was enacted as part of the Affordable Care Act to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an approved biologic. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the reference product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement the BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any product candidate approved in the United States as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider the subject product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If we are unable to obtain marketing approval in jurisdictions outside the United States, we will not be able to market our product candidates outside of the United States.

In order to market and sell THOR-707 or any of our future product candidates in the European Union and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The approval procedure varies among countries and can involve additional testing. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis or at all.

Even if a product candidate we develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any product candidate we develop receives marketing approval, whether as a single agent or in combination with other therapies, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors, and others in the medical community. For example, cancer treatments like chemotherapy, radiation therapy and certain existing immunotherapies are well established in the medical community, and doctors may continue to rely on these therapies. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy, safety and potential advantages compared to alternative treatments;
- the prevalence and severity of any side effects;
- the convenience and ease of administration compared to alternative treatments;
- the clinical indications for which the product candidate is approved;
- the willingness of the target patient population to try new treatments and of physicians to prescribe these treatments;
- the ability to obtain sufficient third-party insurance coverage and adequate reimbursement, including with respect to the use of the approved product as a combination therapy;
- the strength of marketing, sales and distribution support;
- the effectiveness of our sales and marketing efforts;
- the approval of other new products for the same indications; and
- our ability to offer our products, if approved, for sale at competitive prices.

Our operations, including our use of hazardous materials, chemicals, bacteria and viruses, require us to comply with regulatory requirements and expose us to significant potential liabilities.

Our operations involve the use of hazardous materials, including chemicals, and may produce dangerous waste products. Accordingly, we, along with the third parties who will conduct clinical trials and manufacture our products and product candidates on our behalf, are subject to federal, state, local and foreign laws and regulations that govern the use, manufacture, distribution, storage, handling, exposure, disposal and recordkeeping with respect to these materials. We are also subject to a variety of environmental and occupational health and safety laws. Compliance with current or future laws and regulations can require significant costs and we could be subject to substantial fines and penalties in the event of noncompliance. In addition, the risk of contamination or injury from these materials cannot be completely eliminated. In such event, we could be held liable for substantial civil damages or costs associated with the cleanup of hazardous materials.

Our employees, independent contractors, contract research organizations, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud or other illegal activity by our employees, independent contractors, contract research organizations, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to comply with the laws of the FDA and other similar foreign regulatory bodies, provide true, complete and accurate information to the FDA and other similar foreign regulatory bodies, comply with manufacturing standards we have established, comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws, or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs.

Risks Related to Our Dependence on Third Parties

If we fail to comply with our obligations in our agreement with TSRI, we could lose rights that are important to our business.

We rely heavily on the TSRI Agreement pursuant to which we exclusively in-license certain patents and know-how related to our proprietary Expanded Genetic Alphabet platform technology and development programs. The TSRI Agreement imposes, and we may enter into additional agreements, including license agreements, with other parties in the future that impose, diligence, development and commercialization timelines, milestone payments, royalties, insurance and other obligations on us.

The TSRI Agreement gives us exclusive worldwide rights to develop, manufacture, and commercialize certain of TSRI's patent rights, know-how and biological materials relating to our Expanded Genetic Alphabet platform technology. For more information, see "Our License and Collaboration Agreements —License Agreement with TSRI" appearing in Part I, Item 1 of our Annual Report on Form 10-K.

If we fail to comply with our obligations to TSRI under the TSRI Agreement, TSRI may have the right to terminate the TSRI Agreement, in which event we would not be able to develop, obtain regulatory approval for, manufacture or market any product candidate that is covered by the TSRI Agreement, including THOR-707, which would materially harm our business, financial condition, results of operations and growth prospects. Any termination of the TSRI Agreement or reduction or elimination of our rights thereunder may result in our having to negotiate new or reinstated agreements with less favorable terms. Any termination of the TSRI Agreement would cause us to lose our rights to important intellectual property or technology.

We will rely on third parties to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential product candidates.*

We currently depend and will depend in the future upon third parties, including independent investigators, to conduct our clinical trials under agreements with universities, medical institutions, CROs, strategic partners and others. We expect to have to negotiate budgets and contracts with CROs and trial sites, which may result in delays to our development timelines and increased costs.

We currently rely and will rely heavily in the future on third parties over the course of our preclinical studies and clinical trials, and, as a result, will have limited control over the clinical investigators and limited visibility into their day-to-day activities, including with respect to their compliance with the approved clinical protocol. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our

reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with GCP requirements for clinical trials, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these trials or perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP requirements. In addition, our clinical trials must be conducted with biologic product produced under cGMP requirements and may require a large number of patients.

Our failure or any failure by these third parties to comply with the applicable regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting our clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties 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 clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Though we plan to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter 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 prospects.

The manufacturing of biologics is complex and we do not have our own clinical manufacturing capabilities. We will rely on third parties to produce clinical and commercial supplies of any future product candidates.*

We will rely on third-party contract manufacturers to manufacture some of our preclinical product candidate supplies and all of our clinical trial product supplies. We do not own manufacturing facilities for producing any clinical trial product supplies. There can be no assurance that our preclinical and clinical development product supplies will not be limited, interrupted, or of satisfactory quality or continue to be available at acceptable prices. Additionally, the process of manufacturing biologics is complex, highly-regulated and subject to multiple risks. Manufacturing biologics is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions and higher costs. If microbial, viral or other contaminations are discovered at the facilities of our manufacturer, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials, result in higher costs of drug product and adversely harm our business.

We have entered into a contract manufacturing services agreement with third-party manufacturers, pursuant to which we agreed to retain their services for manufacturing process development and to manufacture clinical supply of THOR-707 to cGMP specifications. If these third-party manufacturers are unable to supply us with sufficient clinical grade quantities of THOR-707, and we are unable to timely establish an alternate supply from other third-party contract manufacturers, we will experience delays in our development efforts as we locate and qualify new manufacturers. In particular, any replacement of our manufacturer could require significant effort and expertise because there may be a limited number of qualified replacements or capacity could be limited at each of the qualified replacements. Additionally, we currently rely on single source suppliers for certain of the raw materials for our preclinical and clinical product supplies. If our current or future suppliers are unable to supply us with sufficient raw materials for our preclinical studies and clinical trials, we may experience delays in our development efforts as we locate and qualify new raw material manufacturers. Further, for our combination clinical trial of THOR-707 with an immune checkpoint inhibitor, we will need to procure supply of the immune checkpoint inhibitors for use in the clinical trial. If we are unable to procure sufficient supply from third-party

manufacturers or other sources, we may be required to purchase our supply of checkpoint inhibitors on the open market, which may result in significant additional expense.

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 their standards, such as cGMPs. In the event that any of our manufacturers fail to comply with such requirements or to perform their obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third-party, which we may not be able to do on reasonable terms, if at all. The transfer of the manufacturing of biologic products to a new contract manufacturer can be lengthy and involve significant additional costs. 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. The delays associated with the verification of a new manufacturer would negatively affect our ability to develop product candidates in a timely manner or within budget.

Further, our reliance on third-party manufacturers exposes us to risks beyond our control, including the:

- inability to meet our drug specifications and quality requirements consistently;
- inability to initiate or continue preclinical studies or clinical trials of product candidates under development;
- delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and drug quality issues, including related to scale-up of manufacturing;
- failure to comply with cGMP and similar foreign standards;
- reliance on a limited number of sources, and in some cases, single sources for drug components and raw materials, such that if we are unable to secure a sufficient supply of these drug components and raw materials, we will be unable to manufacture and sell our future product candidate in a timely fashion, in sufficient quantities or under acceptable terms;
- lack of qualified backup suppliers for those components and raw materials that are purchased from a sole or single source supplier;
- inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier or the issuance of an FDA Form 483 notice or warning letter;
- carrier disruptions or increased costs that are beyond our control;
- failure to deliver our drugs under specified storage conditions and in a timely manner; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

Some of these events could be the basis for FDA action, including injunction, recall, seizure, or total or partial suspension of production resulting in failure to begin clinical trials or having to stop ongoing clinical trials. In addition, our third-party manufacturers and suppliers are subject to FDA inspection from time to time. Failure by our third-party manufacturers and suppliers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our product candidate may result in regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses. In addition, our third-party manufacturers and suppliers are subject to numerous environmental, health and safety laws and regulations, including those governing the handling, use, storage, treatment and disposal of waste products, and failure to comply with such laws and regulations could result in significant costs associated with civil or criminal fines and penalties for such third parties. Based on the severity of the regulatory action, our clinical or commercial supply of drug and packaging and other services could be interrupted or limited, which could harm our business.

In addition, our contract manufacturers are or may be engaged with other companies to supply and manufacture materials or products for such companies, which also exposes our suppliers and manufacturers to regulatory risks for the production of such materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may also affect the regulatory clearance of a contract supplier's or manufacturer's facility. If the FDA or a comparable foreign regulatory agency does not approve these facilities for the supply or manufacture of our product candidates, or if it withdraws its approval in the

future, we may need to find alternative supply or manufacturing facilities, which would negatively impact our ability to develop, obtain regulatory approval of or market our product candidates, if approved.

We rely on arrangements pursuant to which we share common services, such as accounting and finance support, with other entities affiliated with Avalon Ventures, an owner of more than 5% of our capital stock.

We have limited internal accounting, finance, human resources and information technology personnel, and we rely on a Support Services Agreement with COI Pharmaceuticals, Inc., or COI, an entity affiliated with Avalon Ventures, pursuant to which we share these services with other Avalon-affiliated entities. While we intend to eventually build out these shared functions internally, we are significantly reliant on COI for these critical business functions at this time. If COI were to terminate the Support Services Agreement with little notice, or otherwise fail to provide these services to us in a timely manner, we may have difficulty continuing our normal business operations. For example, without accounting and finance support provided by COI, we may be unable to meet our reporting obligations to our investors. COI's inability or unwillingness to perform its obligations under the Support Services Agreement could harm our business, prospects, financial condition and results of operations.

We may seek to enter into collaborations or other similar arrangements for our product candidates. If we are unable to enter into such collaborations, or if these collaborations are not successful, our business could be adversely affected.

A part of our strategy is to strategically evaluate and, as deemed appropriate, enter into collaborations in the future on an asset-by-asset basis to maximize the value of each of our programs. We may also enter into collaborations in connection with our platform technology in order to advance the development of programs beyond our initial focus in cytokines. Such collaborations may include the development and commercialization of any of our product candidates or the commercialization of any of our product candidates that are approved for marketing outside the United States. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We have limited capabilities for product development and do not yet have any capability for commercialization. Accordingly, we may enter into collaborations with other companies to provide us with important technologies and funding for our programs and platform technology. We will face significant competition in seeking appropriate collaborators. We may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for any product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view such product candidates as having the requisite potential to demonstrate safety and efficacy. We may also be restricted under future license agreements from entering into agreements on certain terms or at all with potential collaborators.

Collaborations involving our product candidates would pose significant risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or drugs, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such products;
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product

candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

- collaborators may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- collaborators may not provide us with timely and accurate information regarding development, regulatory or commercialization status or results, which could adversely impact our ability to manage our own development efforts, accurately forecast financial results or provide timely information to our stockholders regarding our out-licensed product candidates;
- if a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated; and
- collaborations may be terminated, including for the convenience of the collaborator, and, if terminated, we may find it more difficult to enter into future collaborations or be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as acquisitions of companies, asset purchases and out-licensing or in-licensing of intellectual property, products or technologies. Additional potential transactions that we may consider in the future include a variety of business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any future transactions could increase our near and long-term expenditures, result in potentially dilutive issuances of our equity securities, including our common stock, or the incurrence of debt, contingent liabilities, amortization expenses or acquired in-process research and development expenses, any of which could affect our financial condition, liquidity and results of operations. Future acquisitions may also require us to obtain additional financing, which may not be available on favorable terms or at all. These transactions may never be successful and may require significant time and attention of management. In addition, the integration of any business that we may acquire in the future may disrupt our existing business and may be a complex, risky and costly endeavor for which we may never realize the full benefits of the acquisition. Accordingly, although there can be no assurance that we will undertake or successfully complete any additional transactions of the nature described above, any additional transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for any product candidates we develop or for our Expanded Genetic Alphabet platform technology and other proprietary technologies we may develop, our competitors could develop and commercialize products or technology similar or identical to our products and technology, and our ability to successfully commercialize any product candidates we may develop may be adversely affected.*

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates, Expanded Genetic Alphabet platform technology and other technologies we may develop. We seek to protect our proprietary position by in-licensing intellectual property and filing patent applications in the United States and abroad relating to our product candidates and Expanded Genetic Alphabet platform technology and other proprietary technologies we may develop. Given that the development of our technology and product candidates is at an early stage, our intellectual property portfolio with respect to certain aspects of our technology and product candidates is also at an early stage. For example, we do not own nor have we in-licensed any issued patents directed to the composition of matter of any of the product candidates that we have thus far developed using our Expanded Genetic Alphabet platform technology. We have filed or intend to file patent applications on these aspects of our technology and our product candidates. The patent process is expensive and time consuming, and we may not be able to apply for patents on certain aspects of our platform technology and other technologies we may develop in a timely fashion, at a reasonable cost, in all jurisdictions, or at all. Any patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technology. There is no guarantee that any of our pending patent applications

will result in issued or granted patents, that any of our issued or granted patents will not later be found to be invalid or unenforceable or that any issued or granted patents will include claims that are sufficiently broad to cover our platform technology and other technologies we may develop or to provide meaningful protection from our competitors. Moreover, the patent position of biotechnology and biopharmaceutical companies can be highly uncertain because it involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and product candidates are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely affect our position in the market. 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. Furthermore, in some cases, we have only filed provisional patent applications on certain aspects of our technology and product candidates and each of these provisional patent applications is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of the filing date of the earliest, applicable provisional patent application. Any failure to file a non-provisional patent application within this timeline could cause us to lose the ability to obtain patent protection for the inventions disclosed in the associated provisional patent applications. There can be no assurances that we will seek IP coverage in all the countries where we may wish to commercialize THOR-707 and thus open up the opportunity for others to gain a commercial advantage in these countries.

Composition of matter patents for biological and pharmaceutical products are generally considered to be the strongest form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of use. We cannot be certain, however, that the claims in our pending patent applications, including those claims covering the composition of matter of our product candidates, will be considered patentable by the United States Patent and Trademark Office, or the USPTO, or by patent offices in foreign countries, or that the claims in any of our patents that may issue will be considered valid and enforceable by courts in the United States or foreign countries. Furthermore, in some cases, we may not be able to obtain issued claims covering compositions of matter relating to our product candidates and Expanded Genetic Alphabet platform technology, as well as other technologies that are important to our business, and instead may need to rely on filing patent applications with claims covering a method of use and/or method of manufacture. Method of use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their products for our targeted indications, physicians may prescribe these products "off-label" for those uses that are covered by our method of use patents. Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute. There can be no assurance that any such patent applications will issue as granted patents, and even if they do issue, such patent claims may be insufficient to prevent third parties, such as our competitors, from utilizing our technology. Any failure to obtain or maintain patent protection with respect to our product candidates and Expanded Genetic Alphabet platform technology could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We rely heavily on the TSRI Agreement for the patent rights and know-how required for our Expanded Genetic Alphabet platform technology, which is the underpinning for all our future product candidates.

We rely heavily on the TSRI Agreement for intellectual property rights that are important or necessary to the development of our product candidates and Expanded Genetic Alphabet platform technology. For more information, see "Our License and Collaboration Agreements—License Agreement with TSRI" appearing in Part I, Item 1 of our Annual Report on Form 10-K. The growth of our business may depend in part on our ability to acquire, in-license or use additional third-party intellectual property rights. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Licenses to additional third-party intellectual property, technology and materials that may be required for the development and commercialization of our product candidates or technology may not be available at all or on commercially reasonable terms. In that event, we may be required to expend significant time and resources to redesign our product candidates or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize our future product candidates or technologies, which could materially harm our business, financial condition, results of operations and growth prospects.

Under the TSRI Agreement, TSRI is responsible for prosecution and maintenance of the licensed patents and we are responsible for bringing any actions against any third party for infringing on such patents. We have limited control over the activities that are the responsibility of TSRI under the Agreement. It is possible that TSRI's activities, or the activities of any future licensor, may be less vigorous than had we conducted them ourselves. Furthermore, the TSRI Agreement is subject to, and we expect certain of our future license agreements would also be subject to, a reservation of rights by one or more third parties, including the licensor. In addition, the

TSRI Agreement requires, and we expect certain of our future license agreements would also require, us to meet certain development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products. If we fail to comply with these obligations, we may be required to pay damages and our licensor may have the right to terminate the license, in which event we would not be able to develop or market the products covered by such licensed intellectual property and our competitors or other third parties might be able to gain access to technologies and products that are identical to ours. In addition, such license agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Disputes may arise regarding intellectual property subject to the TSRI Agreement or any of our future license agreements, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe, misappropriate or otherwise violate any intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under the license agreement;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own, which are described below. If we or our licensor fail to adequately protect this intellectual property, our ability to commercialize products could suffer.

In spite of our best efforts, TSRI and any potential future licensors might conclude that we have materially breached our license agreements and might therefore terminate the relevant license agreements, thereby removing our ability develop and commercialize products and technology covered by such license agreements. If any of our current or future inbound license agreements are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations and growth prospects. Our business also would suffer if any current or future licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights.

Our licensors may have relied on third-party consultants or collaborators or on funds from third parties, such as the United States Government, such that our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights or other rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

If any of our owned or in-licensed patent applications do not issue as patents in any jurisdiction, we may not be able to compete effectively.*

Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. With respect to our patent portfolio, as of July 15, 2019, other than one foreign issued patent, all of the patent rights that we own or that we have in-licensed are currently pending patent applications. With respect to both in-licensed and owned intellectual property, we cannot predict whether the patent applications we

and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors or other third parties.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patents and 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 in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors, licensees or partners. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If our current or future licensors, licensees or partners fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our licensors, licensees or partners are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. There may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. We cannot assure you that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it can invalidate a patent or prevent a patent from issuing from a pending patent application. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in any of our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third party patent which might adversely affect our ability to develop and market our products.*

We cannot assure you that our operations do not, or will not in the future, infringe existing or future patents. We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third party patent and pending application in the United States and abroad that is relevant to our therapeutic research programs or necessary for the commercialization of our product candidates and the Expanded Genetic Alphabet platform technology in any jurisdiction.

Numerous U.S. and foreign patents and pending patent applications exist in our market that are owned by third parties, and there may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates and the Expanded Genetic Alphabet platform technology that we may identify. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our products. We do not always conduct independent reviews of pending patent applications of and patents issued to third parties. Patent applications in the United States and elsewhere are typically published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Certain U.S. applications that will not be filed outside the U.S. can remain confidential until patents issue. In addition, patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived. Furthermore, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our products or the use of our products. As such, there may be applications of others now pending or recently revived patents of which we are unaware, potentially relating to our research programs, product candidates and our product candidates and the Expanded Genetic Alphabet platform technology, or their intended uses. These applications may later result in issued patents, or the revival of previously abandoned patents, that will prevent, limit or otherwise interfere with our ability to make, use or sell our products.

The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. We may incorrectly determine that our products are not covered by a third party patent or may incorrectly predict whether a third party's pending application will issue into patents with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which

may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

We cannot provide any assurances that third party patents do not exist which might be enforced against our current technology, including our research programs and product candidates and the Expanded Genetic Alphabet platform technology, their respective methods of use, manufacture and formulations thereof, and could result in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical technology and product candidates would be adversely affected.*

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. Furthermore, even if they are unchallenged, patents in our portfolio may not adequately exclude third parties from practicing relevant technology or prevent others from designing around our claims. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our owned or in-licensed pending and future patent applications may not result in patents being issued which protect our product candidates, Expanded Genetic Alphabet platform technology, or other technologies or which effectively prevent others from commercializing competitive technologies and product candidates. The patent examination process may require us to narrow the scope of the claims of our owned or in-licensed pending or future patent applications, which may limit the scope of patent protection that may be obtained.

No consistent policy regarding the scope of claims allowable in patents in the biotechnology field has emerged in the United States. The patent situation outside of the United States is even more uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions and enforce our intellectual property rights, and more generally could affect the value of our intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell, or importing products that infringe our intellectual property will depend in part on our success in obtaining and enforcing patent claims that cover our technology, inventions and improvements. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our products and the methods used to manufacture those products. Moreover, even our issued patents do not guarantee us the right to practice our technology in relation to the commercialization of our products. The area of patent and other intellectual property rights in biotechnology is an evolving one with many risks and uncertainties, and third parties may have blocking patents that could be used to prevent us from commercializing our patented product candidates and practicing our proprietary technology. Our patents that may issue in the future may be challenged, held to be unenforceable, invalidated, or circumvented, which could limit our ability to stop competitors from marketing related products or limit the length of the term of patent protection that we may have for our product candidates. In addition, the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies. For these reasons, we may have competition for our product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if pending patent applications we own or license issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own or in-license may be challenged, held to be unenforceable, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether our product candidates, Expanded Genetic Alphabet platform technology or other technologies will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and patents that we own or license may be challenged in the courts or patent offices in the United States and abroad. We or our licensors may be subject to a third party preissuance submission of prior art to the USPTO or to foreign patent authorities or become involved in opposition, derivation, revocation, reexamination, post-grant and inter partes review, or interference proceedings or other similar proceedings challenging our owned or licensed patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our owned or in-licensed patent rights, allow third parties to commercialize our product candidates, Expanded Genetic Alphabet platform technology or other technologies and compete directly with us, without payment to

us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. The legal threshold for initiating such proceedings may be low, so that even proceedings with a low probability of success might be initiated. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Moreover, we, or one of our licensors, may have to participate in interference proceedings or derivation proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our or our licensor's priority of invention or other features of patentability with respect to our owned or in-licensed patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our product candidates, Expanded Genetic Alphabet platform technology and other technologies. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us.

If the breadth or strength of protection provided by the patents and patent applications we hold, obtain or pursue with respect to our product candidates is challenged, or if they fail to provide meaningful exclusivity for our product candidates, it could threaten our ability to practice our technologies or commercialize our product candidates. Several patent applications covering our product candidates have been filed recently. We cannot offer any assurances about which, if any, of these patent applications will issue as patents, the breadth of claims in any such patent, or whether the claims of any issued patents will be found invalid, or the patent will be found to be unenforceable, or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or, if applicable in the future, licensed to us could deprive us of rights necessary for the practice of our technologies or the successful commercialization of any product candidates that we may develop. Furthermore, an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications.

We may require the cooperation of our licensors to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Moreover, if we do obtain necessary licenses, we will likely have obligations under those licenses, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license could have a material adverse impact on our business.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful, and issued patents covering our technology and product candidates could be found invalid or unenforceable if challenged.*

Competitors and other third parties may infringe or otherwise violate any issued patents or other intellectual property or the patents or other intellectual property of our licensors. In addition, our patents or the patents of our licensors may become involved in inventorship or priority disputes. Our pending patent applications, which constitute the majority of our patent rights at this time, cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications.

To counter infringement or other unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents or that our patents are invalid or unenforceable. In a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly, decide that the other party's use of our patented technology falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1), or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly, could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. We may find it impractical or undesirable to enforce our intellectual property against some third parties. 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.

If we were to initiate legal proceedings against a third party to enforce a patent directed to our product candidates or Expanded Genetic Alphabet platform technology, or one of our future product candidates, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or insufficient written description. 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 the USPTO or an equivalent foreign body, even outside the context of litigation. Potential proceedings include re-examination, post-grant review, inter partes review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of, or amendment to our patents in such a way that they no longer

cover our technology or any product candidates that we may develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on the applicable product candidates or technology covered by the patent rendered invalid or unenforceable. Such a loss of patent protection would materially harm our business, financial condition, results of operations and prospects.

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 with respect to our patent applications or future patents. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be materially harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology.

Most of our competitors are larger than we are and have substantially greater resources. They are, therefore, likely to be able to sustain the costs of complex patent litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon, misappropriating or otherwise violating our intellectual property rights. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. We may conclude that even if a third party is infringing our issued patent relating to our research programs and product candidates, any patents that may be issued as a result of our pending or future patent applications or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our stockholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims could result in substantial costs and diversion of management resources, which could harm our business. The court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. In addition, the uncertainties associated with litigation could compromise our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, in-license needed technology or other product candidates, or enter into development partnerships that would help us bring our product candidates to market. There could also be public announcements of the results of the hearing, motions, or other interim proceedings or developments. If securities analysts or investors perceive those results to be negative, it could cause the price of shares of our common stock to decline. Any of the foregoing events could harm our business, financial condition, results of operation and prospects.

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

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patent rights, trade secrets, or other intellectual property as an owner, inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. For example, we or our licensors may have inventorship disputes arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of employees, consultants or others who are involved in developing our product candidates, Expanded Genetic Alphabet platform technology or other technologies, or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patent rights, trade secrets or other intellectual property we may develop. If we or our licensors 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, intellectual property that is important to our future success. 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. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Changes in United States patent law or patent jurisprudence could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before we could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent

applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our product candidates, Expanded Genetic Alphabet platform technology, and other proprietary technologies we may develop or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing the claimed invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted, redefine prior art and also may affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies involved in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent United States Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the United States Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated if we fail to comply with these requirements.

Periodic maintenance, renewal fees, and annuity fees, and various other government fees on patents and applications will be due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of our owned or licensed patents and applications. The USPTO and various foreign patent agencies also require compliance with a number of procedural, documentary, fee payment and other similar requirements during the patent application and prosecution process. Noncompliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official communications within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in irrevocable abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If we or our licensors or collaborators fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market with similar or identical products or technology, which would harm our business, financial condition, results of operations and prospects. Further, the standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. As such, we do not know the degree of future protection that we will have on our technologies, products, product candidates or the Expanded Genetic Alphabet platform technology.

Some intellectual property may have been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.

Our in-licensed patent rights from TSRI under the TSRI Agreement were funded in part by the U.S. government and are therefore subject to certain federal regulations. When new technologies are developed with U.S. government funding, the U.S. government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the U.S. government to use the invention or to have others use the invention on its behalf. The U.S. government's rights may also permit it to disclose the funded inventions and technology to third parties and to exercise march-in rights to use or allow third parties to use the technology we have licensed that was developed using U.S. government funding. The U.S. government may exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, or because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to

U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States in certain circumstances and if this requirement is not waived. Any exercise by the U.S. government of such rights or by any third party of its reserved rights could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but 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 from competitive medications, including biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours.

Moreover, in the future we may in-license patent applications or patents that may be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Furthermore, our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

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

Filing, prosecuting, maintaining, defending and enforcing patents on our product candidates, Expanded Genetic Alphabet platform technology, and other proprietary technologies we may develop in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. 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 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 drugs or technology and may export otherwise infringing drugs or technology to territories where we have patent protection, but enforcement rights are not as strong as those in the United States. These drugs may compete with our product candidates 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 do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Similarly, if our trade secrets are disclosed in a foreign jurisdiction, competitors worldwide could have access to our proprietary information and we may be without satisfactory recourse. Such disclosure could have a material adverse effect on our business. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

The requirements for patentability differ, in varying degrees, from country to country, and the laws of some foreign countries do not protect intellectual property rights, including trade secrets, to the same extent as federal and state laws of the U.S. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions. Many countries, including European Union countries, India, Japan and China, have compulsory licensing laws under which a patent owner may be compelled under specified circumstances to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In those countries, patents provide little to no benefit, and we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. 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, which could adversely affect our business, financial condition, results of operations and prospects.

If we do not obtain patent term extension and/or data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our owned or in-licensed U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension, or PTE, of up to five years as compensation for patent term lost during the FDA regulatory review process. A PTE cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar patent term restoration provisions to compensate for commercialization delay caused by regulatory review are also available in certain foreign countries and territories, such as in Europe under a Supplementary Patent Certificate, or SPC. Such laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. However, we may not be granted an extension in the United States and/or foreign countries and territories because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is shorter than what we request, our competitors may obtain approval of competing products following our patent expiration, and may take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to launch their product earlier than might otherwise be the case, and our business, financial condition, results of operations and prospects could be materially harmed.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology and other proprietary information and to maintain our competitive position. Elements of our products and product candidates, including processes for their preparation and manufacture, may involve proprietary know-how, information, or technology that is not covered by patents, and thus for these aspects we may consider trade secrets and know-how to be our primary intellectual property. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market. Because we expect to rely on third parties in the development and manufacture of our product candidates, we must, at times, share trade secrets with them. Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Trade secrets and know-how can be difficult to protect. We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements, materials transfer agreements and similar agreements with parties who have access to them, such as our employees, collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees, consultants and outside collaborators. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. We cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology and processes. We cannot be certain 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. Despite these efforts and the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our products that we consider proprietary. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Trade secrets will over time be disseminated within the industry through independent development, the publication of journal articles and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. Though our agreements with third parties typically restrict the ability of our advisors, employees, collaborators, licensors, suppliers,

third-party contractors and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. Because from time to time we expect to rely on third parties in the development, manufacture, and distribution of our products and provision of our services, we must, at times, share trade secrets with them. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

Third-party claims of intellectual property infringement, misappropriation or other violation against us, our licensors or our collaborators may prevent or delay the development and commercialization of our product candidates and Expanded Genetic Alphabet platform technology.

The field of immunotherapies is competitive and dynamic. Due to the focused research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is in flux, and it may remain uncertain in the future. As such, there may be significant intellectual property related litigation and proceedings relating to our owned and in-licensed, and other third party, intellectual property and proprietary rights in the future.

Our commercial success depends in part on our and our licensors' ability to avoid infringing, misappropriating and otherwise violating the patents and other intellectual property rights of third parties. There is a substantial amount of complex litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. Such litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and, even if resolved in our favor, is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are developing our product candidates, and our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained, or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use, and the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. We cannot assure you that our product candidates, Expanded Genetic Alphabet platform technology, and other proprietary technologies we may develop will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already been issued and that a third party, for example, a competitor in the fields in which we are developing our product candidates, might assert are infringed by our current or future product candidates, including claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our product candidates. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates, Expanded Genetic Alphabet platform technology, and other proprietary technologies we may develop, could be found to be infringed by our product candidates. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit.

The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability or priority. A court of competent jurisdiction could hold that third-party patents asserted against us are valid, enforceable and infringed, which could materially and adversely affect our ability to commercialize any product candidates we may develop and any other product candidates or technologies covered by the asserted third-party patents. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity may be difficult. In order to successfully challenge the validity of any U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe, misappropriate or otherwise violate a third party's intellectual property rights, and we are unsuccessful in demonstrating that such rights are invalid or unenforceable, we could be required to obtain a license from such a third party in order to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease

commercializing the infringing technology or product. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, and could divert the time and attention of our technical personnel and management, cause development delays, and/or require us to develop non-infringing technology, which may not be possible on a cost-effective basis. In the event of a successful claim of infringement against us, we may have to pay substantial monetary damages, including treble damages and attorneys' fees for willful infringement, pay royalties and other fees, redesign our infringing drug or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. Any of the foregoing events would harm our business, financial condition, results of operations and prospects.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, we may not have sufficient resources to bring these actions to a successful conclusion. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. Further, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and 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. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately, as such litigation or proceedings could last for years before they are concluded. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace, including compromising our ability to raise the funds necessary to advance our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development collaborations that would help us commercialize our product candidates, if approved. Any of the foregoing events would harm our business, financial condition, results of operations and prospects.

We may not be successful in obtaining any necessary rights to our product candidates or technologies.

We currently have rights to intellectual property covering our product candidates, Expanded Genetic Alphabet platform technology, and other proprietary technologies we may develop. Other pharmaceutical companies and academic institutions may also have filed or are planning to file patent applications potentially relevant to our business. In order to avoid infringing these third-party patents, we may find it necessary or prudent to obtain licenses to such patents from such third-party intellectual property holders. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for our product candidates, Expanded Genetic Alphabet platform technology, and other proprietary technologies we may develop. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. 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 it to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may be subject to claims that our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.*

Many of our employees, consultants, and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors and potential competitors. Although we have policies in place to try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we caused an individual to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. 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, and a court could prohibit us from using technologies or features that are essential to our product candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the current or former employers. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each

of which would have an adverse effect on our business, results of operations and financial condition. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

We currently do not own any registered trademarks. We currently have a pending trademark application in the United States for SYNTHORIN and a pending application for the SYNTHORX logo. We also have pending trademark applications in the United States and several foreign countries for the SYNTHORX mark. Our unregistered trademarks or trade names or, following registration, registered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. During trademark registration proceedings we may receive rejections of our applications by the USPTO or in other foreign jurisdictions. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Moreover, any name we have proposed to use with our product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, it may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark.

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 or other third parties 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 registered or unregistered trademarks or trade names. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks. Over the long term, if we are unable to 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 affect our business, financial condition, results of operations and prospects.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to our product candidates or utilize similar technology but that are not covered by the claims of the patents that we license or may own;
- we, or our current or future licensors might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or own, now or in the future;
- we, or our current or future licensors, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights, including by invalidating, circumventing or designing around our patent rights;

- it is possible that our current or future pending owned or licensed patent applications will not lead to issued patents;
- we cannot predict the scope of protection of any patent issuing based on our patent applications, including whether the patent applications that we own or in-license will result in issued patents with claims that cover our product candidates or the Expanded Genetic Alphabet platform technology or uses thereof in the United States or in other foreign countries;
- the claims of any patent issuing based on our patent applications may not provide protection against competitors or any competitive advantages, or may be challenged by third parties;
- if enforced, a court may not hold that our patents are valid, enforceable and infringed;
- issued patents that we may hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business, including if others obtain patents claiming subject matter similar to or improving that covered by our patents and patent applications;
- we may need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property; and
- we may fail to adequately protect and police our trademarks and trade secrets.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Legal and Regulatory Compliance Matters

We are very early in our development process and future legislation and/or regulations and policies adopted by the FDA, the EMA or similar regulatory authorities may increase the time and cost required for us to initiate, conduct, and complete clinical trials of our current and potential product candidates.

The FDA has established regulations to govern the drug and biologic development and approval process, as have foreign regulatory authorities. The policies of the FDA and other regulatory authorities may change and additional laws may be enacted or government regulations may be promulgated that could prevent, limit, delay, or alternatively accelerate regulatory review of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the current U.S. President's administration may impact our business and industry. Namely, the current U.S. President's administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these orders will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose restrictions on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

We may seek orphan drug designation for some or all of our product candidates across various indications, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug designation, including market exclusivity, which may cause our revenue, if any, to be reduced.

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. In order to obtain orphan drug designation, the request must be made before submitting a BLA. In the United States, orphan drug designation

entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval of that particular product for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a BLA, to market the same biologic (meaning, a product with the same principal molecular structural features) for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan drug exclusivity or if FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. As a result, even if one of our product candidates receives orphan exclusivity, the FDA can still approve other biologics that do not have the same principal molecular structural features for use in treating the same indication or disease or the same biologic for a different indication or disease during the exclusivity period. Furthermore, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product or if a subsequent applicant demonstrates clinical superiority over our product.

We may seek orphan drug designation for some or all of our product candidates in specific orphan indications in which there is a medically plausible basis for the use of these products. Even if we obtain orphan drug designation, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition, or if a subsequent applicant demonstrates clinical superiority over our products, if approved. In addition, although we may seek orphan drug designation for other product candidates, we may never receive such designations.

A fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

We may seek fast track designation for some of our product candidates, including our IL-2 Synthorins. If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the product sponsor may apply for FDA fast track designation. The FDA has broad discretion whether or not to grant this designation, and even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

Any breakthrough therapy designation that we may receive from the FDA for our product candidates 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 breakthrough therapy designation for some of our product candidates, including our IL-2 Synthorins. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. For drugs 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 while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also 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 make such designation. The availability of breakthrough therapy designation was established with the passage of the Food and Drug Administration Safety and Innovation Act of 2012. We cannot be sure that any evaluation we may make of our product candidates as qualifying for breakthrough therapy designation will meet the FDA's expectations. 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 as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Even if we obtain regulatory approval for any product candidates, they will remain subject to ongoing regulatory oversight.

Any product candidate for which we obtain marketing approval will also be subject to ongoing regulatory requirements for labeling, packaging, storage, distribution, advertising, promotion, record-keeping and submission of safety and other post-marketing information. For example, approved products, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs. As such, we and our contract manufacturers will be subject to continual review and periodic inspections to assess compliance with cGMPs. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing and quality control. Any regulatory approvals that we receive may also be subject to a REMS plan, limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 trials, and surveillance to monitor the quality, safety and efficacy of the drug. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval. We will also be required to report certain adverse reactions and production problems, if any, to the FDA and to comply with requirements concerning advertising and promotion for our products. Further, we will be required to comply with FDA promotion and advertising rules, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved uses, known as off-label use, limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet and social media.

Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party suppliers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention, or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties and other sanctions.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include:

- The U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. The term remuneration has been interpreted broadly to include anything of value. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.
- The U.S. federal false claims and civil monetary penalties laws, including the civil False Claims Act, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

- The U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and their respective implementing regulations, which also imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information.
- The Federal Food, Drug and Cosmetic Act, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices.
- The U.S. Public Health Service Act, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product.
- The Physician Payments Sunshine Act, and its implementing regulations, which requires certain manufacturers of drugs, biologics and certain other products that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to CMS information related to certain payments and transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.
- Analogous U.S. state and local laws and regulations, including: state anti-kickback and false claims laws, which may apply to claims involving healthcare items or services reimbursed by any third-party payor, including private insurers our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers professionals and entities and other potential referral sources; state and local laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; state and local laws that require the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.
- Similar healthcare laws and regulations in the European Union and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, additional integrity reporting and oversight obligations, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations, any of which could harm our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

Healthcare legislative or regulatory reform measures may have a negative impact on our business and results of operations.*

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, ACA was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things: (i) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations; (ii) established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs; (iii) expanded the availability of lower pricing under the 340B drug pricing program by adding new entities to the program; (iv) increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP; (v) expanded the eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; (vi) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and (vii) established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drugs.

Some of the provisions of the ACA have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017, or the Tax Act, included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans and the annual fee imposed on certain health insurance providers based on market share. The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In July 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of the ACA, and because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. While neither the Texas District Court Judge, Trump administration nor CMS have stated that the ruling will have an immediate effect, it is unclear how this decision, subsequent appeals, if any, and other efforts will impact the ACA. We continue to evaluate the potential impact of the ACA and its possible repeal or replacement on our business.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further 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. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have an adverse effect on customers for our product candidates, if approved, and, accordingly, our financial operations.

Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent 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 products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Further, the Trump administration released a "Blueprint", or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. HHS has started soliciting feedback on some of these measures and, at the same, has implemented others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019. While some measures will require authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

Additionally, at the state level, legislatures are increasingly passing legislation and implementing 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.

We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs.

In addition, FDA regulations and guidance may be revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. The Trump administration has also taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these requirements will be interpreted and implemented and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose restrictions on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. Any new regulations or guidance, or revisions or reinterpretations of existing regulations or guidance, may impose additional costs or lengthen FDA review times for our future product candidates. We cannot determine how changes in regulations, statutes, policies, or interpretations when and if issued, enacted or adopted, may affect our business in the future. If such changes result in significant costs or delays in receipt of, or failure to receive, regulatory approvals for any of our product candidates, our business, financial condition, and results of operations would be adversely affected.

Our business activities may be subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery and anti-corruption laws.

Our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, and in the future will require interacting with officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently the Securities and Exchange Commission, or SEC, and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents, suppliers, manufacturers, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of facilities, including those of our suppliers and manufacturers, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries as well as difficulties in manufacturing or continuing to develop our products, and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

We are subject to extensive laws and regulations related to data privacy, and our failure to comply with these laws and regulations could harm our business.

We are subject to laws and regulations governing data privacy and the protection of 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. There are foreign and state law versions of these laws and regulations to which we are currently and/or may in the future, be subject. For example, the collection and use of personal health data in the European Union is governed by the GDPR. The GDPR, which is wide-ranging in scope, imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, the security and confidentiality of the personal data, data breach notification and the use of third party processors in connection with the processing of personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union to the United States, provides an enforcement authority and imposes large monetary penalties for noncompliance. The GDPR requirements apply not only to third-party transactions, but also to transfers of information within our company, including employee information. The GDPR and

similar data privacy laws of other jurisdictions place significant responsibilities on us and create potential liability in relation to personal data that we or our third party service providers process, including in clinical trials conducted in the United States and the European Union. In addition, we expect that there will continue to be new proposed laws, regulations and industry standards relating to privacy and data protection in the United States, the European Union and other jurisdictions, and we cannot determine the impact such future laws, regulations and standards may have on our business.

Additionally, California recently enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. When it goes into effect on January 1, 2020, the CCPA will require covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. Legislators have stated that amendments will be proposed to the CCPA before it goes into effect, but it remains unclear what, if any, modifications will be made to this legislation or how it will be interpreted. As currently written, the CCPA will likely impact (possibly significantly) our business activities and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information.

U.S. federal income tax reform could adversely affect us.

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Code. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses generated after December 31, 2017 to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. We do not expect this tax legislation to have a material impact to our current projection of minimal cash taxes for the near future. However, we continue to examine the impact that this tax legislation may have on our business in the longer term. Accordingly, notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the newly enacted federal tax law. The impact of this tax legislation on holders of our common stock is also uncertain and could be adverse.

Our business could be adversely affected by changes as a result of the current U.S. presidential administration.

President Trump has imposed, and has publicly stated that he may continue to impose, importation tariffs from certain countries such as China and Mexico, which could affect the cost of certain of raw materials used in the production of our product candidates. In addition, the Trump Administration has appointed and employed many new secretaries, directors and the like into positions of authority in the U.S. Federal government dealing with the pharmaceutical and healthcare industries that may potentially have a negative impact on the prices and the regulatory pathways for certain pharmaceutical products such as those developed by us. Such changes in the regulatory pathways could adversely affect and or delay our ability to market and sell our products in the U.S.

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, including as recently as January 2019, 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. 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, in our operations as a public company, 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.

Risks Related to Our Business Operations, Employee Matters and Managing Growth

Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

We are highly dependent on the management, research and development, clinical, financial and business development expertise of our executive officers, as well as the other members of our scientific and clinical teams. Although we have employment offer letters which outline the terms of employment with each of our executive officers, each of them may terminate their employment with us at any time. As such, these employment offer letters do not guarantee our retention of our executive officers for any period of time. We do not maintain "key person" insurance for any of our employees.

Recruiting and retaining qualified scientific and clinical personnel and, if we are successful in obtaining marketing approval for our product candidates, sales and marketing personnel, is critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval for and commercialize our product candidates. We are based in the Greater San Diego Area, a region that is home to many other biopharmaceutical companies as well as many academic and research institutions, resulting in fierce competition for qualified personnel. Furthermore, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited, and could harm our business, prospects, financial condition and results of operations.

We expect to grow our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.*

As of June 30, 2019, we had 43 full-time employees. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical development, regulatory affairs, finance and, if any of our product candidates receive marketing approval, sales, marketing and distribution. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities to devote time to managing these growth activities. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. Our inability to effectively manage the expansion of our operations may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our potential ability to generate revenue could be reduced and we may not be able to implement our business strategy.

Our internal computer systems, or those used by our CROs or other contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems, and those of our CROs and other third parties, such as COI, on which we rely or will rely, are vulnerable to damage from computer viruses and unauthorized access, malware, natural disasters, fire, terrorism, war and telecommunication, electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. While we have not experienced any such material system failure or security breach to our knowledge to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of preclinical data or data from future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we plan to rely on third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. 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 and the further development and commercialization of our future product candidates could be delayed.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We rely on third-party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers were affected by a man-made or natural disaster or other business interruption. In addition, our corporate headquarters is located in the Greater San Diego Area near major earthquake faults and fire zones, and the ultimate impact on us of being located near major earthquake faults and fire zones and being consolidated in a certain geographical area is unknown. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

A variety of risks associated with marketing our product candidates internationally, if approved, could materially adversely affect our business.

We plan to seek regulatory approval of our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- regulatory requirements in foreign countries that differ from those in the United States;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- complexities associated with managing multiple payor reimbursement regimes, government payors or patient self-pay systems;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

Any of these factors could harm our future international expansion and operations and, consequently, our results of operations.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. A severe or prolonged global economic downturn could result in a variety of risks to our business, including our ability to raise additional capital when needed on acceptable terms, if at all. This is particularly true in Europe, which is undergoing a continued severe economic crisis. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

The United Kingdom's referendum to leave the European Union or "Brexit," has and may continue to cause disruptions to capital and currency markets worldwide. The full impact of the Brexit decision, however, remains uncertain. A process of negotiation will determine the future terms of the United Kingdom's relationship with the European Union. During this period of negotiation, our results of operations and access to capital may be negatively affected by interest rate, exchange rate and other market and economic volatility, as well as regulatory and political uncertainty. Brexit may also have a detrimental effect on our suppliers and manufacturers, which would, in turn, adversely affect our financial condition.

Risks Related to the Securities Markets and Ownership of Our Common Stock

An active trading market for our common stock may not continue to be developed or be sustained, which may make it difficult for you to sell your shares.

Prior to our initial public offering in December 2018, there had been no public market for our common stock. The trading market for our common stock on The Nasdaq Global Select Market has been limited and an active trading market for our shares may not be sustained. If an active market for our common stock is not sustained, it may be difficult for you to sell your shares at a price that is attractive to you, or at all.

The price of our common stock could be subject to volatility related or unrelated to our operations.

Our stock price may be volatile. The stock market in general and the market for biotechnology and pharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your shares at a price that is attractive to you, or at all. The market price for our common stock may be influenced by many factors, including:

- adverse results from preclinical studies;
- the commencement, enrollment or results of any future clinical trials we may conduct, or changes in the development status of our product candidates;
- adverse results from, delays in or termination of clinical trials;
- unanticipated serious safety concerns related to the use of our product candidates;
- clinical trial results from, or regulatory approval of, a competitor's product candidate;
- adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;
- any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- lower than expected market acceptance of our product candidates following approval for commercialization;
- adverse developments concerning our manufacturers;
- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- introduction of new products or services by our competitors;
- changes in financial estimates by us or by any securities analysts who might cover our stock;
- conditions or trends in our industry;
- our cash position;
- sales of our common stock by us or our stockholders in the future;
- adoption of new accounting standards;

- ineffectiveness of our internal controls;
- changes in the market valuations of similar companies;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biotechnology and pharmaceutical industry;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- investors' general perception of our company and our business;
- recruitment or departure of key personnel;
- overall performance of the equity markets;
- trading volume of our common stock;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies and product candidates;
- significant lawsuits, including patent or stockholder litigation;
- changes in the structure of healthcare payment systems;
- proposed changes to healthcare laws or pharmaceutical pricing in the United States or foreign jurisdictions, or speculation regarding such changes;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

If securities or industry analysts do not publish research or reports about our company, or if they issue unfavorable or inaccurate research regarding our business, our share price and trading volume could decline.

The trading market for our common stock depends 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 covers us downgrades our stock or publishes unfavorable or inaccurate research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

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

Certain of our executive officers, directors and large stockholders own a significant percentage of our outstanding capital stock. As of June 30, 2019, our executive officers, directors, holders of 5% or more of our common stock and their respective affiliates beneficially owned in the aggregate approximately 87.0% of our outstanding common stock. As a result of their share ownership, these stockholders may have the ability to influence our management and policies and will be able to significantly affect the outcome of matters requiring stockholder approval such as elections of directors, amendments of our organizational documents or approvals of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that our stockholders may feel are in their best interest.

If our stockholders sell substantial amounts of our common stock, the market price of our common stock could decline.*

The price of our common stock could decline if there are substantial sales of our common stock, particularly sales by our directors, executive officers and significant stockholders, or if there is a large number of shares of our common stock available for sale and the market perceives that sales will occur. All of our outstanding shares of common stock are available for sale in the public market, subject only to the restrictions of Rule 144 under the Securities Act in the case of our affiliates.

In addition, we have filed a registration statement on Form S-8 under the Securities Act of 1933, as amended, or the Securities Act, registering the issuance of 6,473,865 shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under the registration statement on Form S-8 are available for sale in the public market subject to vesting arrangements and exercise of options, and the restrictions of Rule 144 in the case of our affiliates.

Additionally, certain holders of our common stock, or their transferees, have rights, subject to some conditions, to require us to file one or more registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If we were to register the resale of these shares, they could be freely sold in the public market. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, the terms of any future debt agreements may preclude us from paying dividends. Any return to stockholders will therefore be limited in the foreseeable future to the appreciation of their stock.

We incur significant increased costs as a result of operating as a public company, and our management is required to devote substantial time to public company reporting and compliance initiatives.

As a public company listed on the Nasdaq Global Select Market, we incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which requires, among other things, that we file with the Securities and Exchange Commission, or the SEC, annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and The Nasdaq Global Select Market to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We are an "emerging growth company," and the reduced disclosure requirements applicable to "emerging growth companies" may make our common stock less attractive to investors.

We are an "emerging growth company" as defined in the JOBS Act, and, therefore, we may take advantage of reduced disclosure and regulatory requirements that are otherwise generally applicable to public companies, including presenting only two years of audited financial statements and related financial disclosure, not being required to have our internal control over financial reporting audited by our independent registered public accounting firm pursuant to Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments. We may take advantage of these reduced disclosure and regulatory requirements until we are no longer an "emerging growth company." We may remain an "emerging growth company" until as late as December 31, 2023 (the fiscal year-end following the fifth anniversary of the completion of our initial public offering), although we may cease to be an "emerging growth company" earlier under certain circumstances, including if the market value of our common stock that is held by non-affiliates exceeds $700 million as of any December 31, in which case we would cease to be an "emerging growth company" as of the following December 31, or if our gross revenue exceeds $1.07 billion in any fiscal year. In addition, the JOBS Act provides that an emerging growth company can delay adopting new or revised accounting standards until those standards apply to private companies. We have irrevocably elected not to avail ourselves of this delayed adoption of new or revised accounting standards and, therefore, we are subject to the same new or revised accounting standards as public companies that are not emerging growth companies.

The exact implications of the JOBS Act are still subject to interpretations and guidance by the SEC and other regulatory agencies, and we may not be able to take advantage of all of the benefits of the JOBS Act. In addition, investors may find our common stock less attractive if we rely on the exemptions and relief granted by the JOBS Act. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our share price may decline or become more volatile.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company" which would allow us to take advantage of many of the same exemptions from disclosure requirements including exemption from compliance with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

If we fail to maintain an effective system of disclosure controls and internal control over financial reporting, our ability to produce timely and accurate financial statements or comply with applicable regulations could be impaired.

As a public company, we are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of the applicable listing standards of the Nasdaq Global Select Market. We expect that the requirements of these rules and regulations will continue to increase our legal, accounting and financial compliance costs, make some activities more difficult, time-consuming and costly and place significant strain on our personnel, systems and resources. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We are continuing to develop and refine our disclosure controls and other procedures that are designed to ensure that information required to be disclosed by us in the reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms and that information required to be disclosed in reports under the Exchange Act is accumulated and communicated to our principal executive and financial officers. We are also continuing to improve our internal control over financial reporting. In order to develop, maintain and improve the effectiveness of our disclosure controls and procedures and internal control over financial reporting, we have expended, and anticipate that we will continue to expend, significant resources, including accounting-related costs and significant management oversight.

Our current controls and any new controls that we develop may become inadequate because of changes in conditions in our business. Further, weaknesses in our disclosure controls and internal control over financial reporting may be discovered in the future. Any failure to develop or maintain effective controls or any difficulties encountered in their implementation or improvement could harm our results of operations or cause us to fail to meet our reporting obligations and may result in a restatement of our consolidated financial statements for prior periods. Any failure to implement and maintain effective internal control over financial reporting could also adversely affect the results of periodic management evaluations and annual independent registered public accounting firm attestation reports regarding the effectiveness of our internal control over financial reporting that we will eventually be required to include in our periodic reports that will be filed with the SEC. Ineffective disclosure controls and procedures and internal control over financial reporting could also cause investors to lose confidence in our reported financial and other information, which would likely have a negative effect on the trading price of our common stock. In addition, if we are unable to continue to meet these requirements, we may not be able to remain listed on the Nasdaq Global Select Market. We are not currently required to comply with the SEC rules that implement Section 404 of the Sarbanes-Oxley Act and are therefore not required to make a formal assessment of the effectiveness of our internal control over financial reporting for that purpose. As a public company, we will be required to provide an annual management report on the effectiveness of our internal control over financial reporting commencing with our second annual report on Form 10-K.

Any failure to maintain effective disclosure controls and internal control over financial reporting could have a material and adverse effect on our business, results of operations and financial condition and could cause a decline in the trading price of our common stock.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our certificate of incorporation and bylaws that may make it difficult for a third-party to acquire, or attempt to acquire, control of our company, even if a change in control was considered favorable by our stockholders.

Our charter documents also contain other provisions that could have an anti-takeover effect, such as:

- establishment of a classified board of directors so that not all members of our board of directors are elected at one time;
- permitting the board of directors to establish the number of directors and fill any vacancies and newly created directorships;
- providing that directors may only be removed for cause and by a two-thirds majority vote of the stockholders;
- prohibiting cumulative voting for directors;
- requiring super-majority voting to amend some provisions in our certificate of incorporation and bylaws;
- authorizing the issuance of "blank check" preferred stock that our board of directors could use to implement a stockholder rights plan;
- eliminating the ability of stockholders to call special meetings of stockholders; and
- prohibiting stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibit a person who owns 15% or more of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. Any provision in our certificate of incorporation or our bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and, to the extent enforceable, the federal district courts of the United States of America will be the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.*

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: any derivative action or proceeding brought on our behalf; any action asserting a breach of a fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, 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. Our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees. By becoming a stockholder in our company, you will be deemed to have notice of and have consented to the provisions of our amended and restated certificate of incorporation related to choice of forum, but will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder. However a court may determine that these provisions are unenforceable. If a court were to find either choice of forum provisions contained in our amended and 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. For example, the Court of Chancery of the State of Delaware recently determined that the exclusive forum provision of federal district courts of the United States of America for resolving any complaint asserting a cause of action arising under the Securities Act is not enforceable. However, this decision may be appealed and may be ultimately overturned by the Delaware Supreme Court. In light of the recent Court of Chancery decision, we do not currently intend to enforce the foregoing federal forum selection provision unless the decision is reversed on appeal.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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

Use of Proceeds

On December 6, 2018, we commenced our initial public offering pursuant to a registration statement on Form S-1 (File No. 333-228355) that was declared effective by the SEC on December 6, 2018, for 11,912,727 shares of our common stock for sale to the public at a price of $11.00 per share. In addition, in December 2018, the underwriters exercised their over-allotment option to purchase 1,786,909 additional shares of our common stock in the initial public offering at the public offering price of $11.00 per share, such that the aggregate offering price of our initial public offering was $150.7 million. The net offering proceeds to us, after deducting underwriting discounts and commissions and offering costs, were $137.5 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10% or more of any class of our equity securities or to any other affiliates. The underwriters for our initial public offering were Jefferies LLC, SVB Leerink LLC (formerly Leerink Partners LLC), Evercore Group LLC and H.C. Wainwright & Co., LLC.

There has been no material change in the use of proceeds from our initial public offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) on December 7, 2018. Through the date hereof, we have used approximately $30.0 million of the net proceeds from the offering. Pending such uses, we have, and plan to continue to invest the balance of the net proceeds from this offering in short- and intermediate-term investments in accordance with our investment policy. These investments may include money market funds and investment securities consisting of U.S. Treasury notes, and high quality, marketable debt instruments of corporations and government sponsored enterprises.

ITEM 3. Defaults Upon Senior Securities.

None.

ITEM 4. Mine Safety Disclosures.

Not applicable.

ITEM 5. Other Information.

None.

ITEM 6. Exhibits

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed December 11, 2018).
3.2	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K, filed December 11, 2018).
4.1	Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-228355), filed November 27, 2018).
4.2	Amended and Restated Investors' Rights Agreement, dated April 12, 2018, by and among the Registrant and certain of its securityholders, as amended (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-228355), filed November 13, 2018).
31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18.U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes Oxley Act of 2002.
101.INS	XBRL Instance Document.
101.SCH	XBRL Taxonomy Extension Schema Document.
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.

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.

Synthorx, Inc.

Date: August 1, 2019

By: /s/ Laura Shawver, Ph.D.

Laura Shawver, Ph.D.
President & Chief Executive Officer
(on behalf of the registrant and as the registrant's Principal Executive Officer)

/s/ Tighe Reardon

Tighe Reardon
Acting Chief Financial Officer
(on behalf of the registrant and as the registrant's Principal Accounting Officer)

Exhibit 31.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Laura Shawver, certify that:

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

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

3. Based on my knowledge, the consolidated 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(s) 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)) 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) 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

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

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

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

/s/ Laura Shawver, Ph.D.
Laura Shawver, Ph.D.
President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: August 1, 2019

Exhibit 31.2

CERTIFICATION OF THE CHIEF FINANCIAL OFFICER PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Tighe Reardon, certify that:

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

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

3. Based on my knowledge, the consolidated 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(s) 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)) 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) 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

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

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

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

/s/ Tighe Reardon
Tighe Reardon
Acting Chief Financial Officer
(Principal Financial Officer)

Date: August 1, 2019

Exhibit 32.1

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

In connection with the Quarterly Report on Form 10-Q of Synthorx, Inc. (the "Company") for the quarterly period ended June 30, 2019, to which this Certification is attached, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company herby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to their knowledge:

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

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

The undersigned have executed this Certification effective as of August 1, 2019.

/s/ Laura Shawver, Ph.D.
Laura Shawver, Ph.D.
President, Chief Executive Officer and Director
(Principal Executive Officer)

/s/ Tighe Reardon
Tighe Reardon
Acting Chief Financial Officer
(Principal Financial Officer)

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. § 1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference into any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing. 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.