UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2022

OR

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

For the transition period from _____ to _____

Commission file number: 001-36327

Neoleukin Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**98-0542593**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

188 East Blaine Street, Suite 450
Seattle, Washington 98102
(Address of principal executive offices, including zip code)
(Registrant's telephone number, including area code): (866) 245-0312

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 $0.000001	**NLTX**	**The Nasdaq Global 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 during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

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

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

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

As of November 11, 2022, there were 42,594,602 shares of the registrant's common stock outstanding.

NEOLEUKIN THERAPEUTICS, INC.

Quarterly Report on Form 10-Q

For the Quarter Ended September 30, 2022

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Except as otherwise indicated herein or as the context otherwise requires, references in this report to, "the Company," "we," "us," "our" and similar references refer to Neoleukin Therapeutics, Inc. (formerly Aquinox Pharmaceuticals, Inc.), a Delaware corporation. The name "Neoleukin" is a trademark of the Company in the United States. This report also contains references to registered marks, trademarks, and trade names of other companies that are property of their respective holders.

PART I. FINANCIAL INFORMATION

Item 1. Condensed Financial Statements

NEOLEUKIN THERAPEUTICS, INC.

Condensed Balance Sheets
(Unaudited)
(In thousands of U.S. dollars, except per share and share amounts)

	September 30, 2022	December 31, 2021
Assets		
Current assets		
Cash and cash equivalents	$ 40,335	$ 142,467
Short-term investments	66,543	—
Other current assets	1,979	1,522
Total current assets	108,857	143,989
Property and equipment, net	5,817	6,452
Operating lease right-of-use assets	9,990	10,766
Intangible asset, net	—	128
Other non-current assets	1,912	1,928
Total assets	$ 126,576	$ 163,263
Liabilities		
Current liabilities		
Accounts payable and accrued liabilities	$ 8,858	$ 7,415
Operating lease liabilities	1,320	1,166
Finance lease liabilities	59	55
Total current liabilities	10,237	8,636
Non-current operating lease liabilities	10,683	11,696
Non-current finance lease liabilities	9	67
Total liabilities	20,929	20,399
Stockholders' equity		
Common stock - $0.000001 par value - authorized, 100,000,000 as of September 30, 2022 and December 31, 2021; issued and outstanding, 42,594,602 as of September 30, 2022 and 42,457,471 as of December 31, 2021	—	—
Preferred stock - $0.000001 par value - authorized, 5,000,000 as of September 30, 2022 and December 31, 2021; issued and outstanding, 0 as of September 30, 2022 and December 31, 2021	—	—
Additional paid-in capital	543,348	536,362
Accumulated other comprehensive income (loss)	(92)	—
Accumulated deficit	(437,609)	(393,498)
Total stockholders' equity	105,647	142,864
Total liabilities and stockholders' equity	$ 126,576	$ 163,263

The accompanying notes form an integral part of these condensed financial statements.

NEOLEUKIN THERAPEUTICS, INC.

Condensed Statements of Operations and Comprehensive Income (Loss)
(Unaudited)
(In thousands of U.S. dollars, except per share and share amounts)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Operating expenses				
Research and development	$ 9,471	$ 9,896	$ 31,128	$ 29,402
General and administrative	4,138	5,556	13,718	16,122
Total operating expenses	13,609	15,452	44,846	45,524
Loss from operations	(13,609)	(15,452)	(44,846)	(45,524)
Interest income	559	6	766	14
Other income (loss), net	(22)	—	(32)	(15)
Net loss	$ (13,072)	$ (15,446)	$ (44,112)	$ (45,525)
Comprehensive income (loss):				
Unrealized loss on available-for-sale securities	(20)	—	(92)	—
Comprehensive loss	$ (13,092)	$ (15,446)	$ (44,204)	$ (45,525)
Net loss per share – basic and diluted	$ (0.24)	$ (0.28)	$ (0.80)	$ (0.83)
Basic and diluted weighted average common shares outstanding	55,251,039	55,087,777	55,199,822	55,020,059

The accompanying notes form an integral part of these condensed financial statements.

NEOLEUKIN THERAPEUTICS, INC.

Condensed Statements of Cash Flows
(Unaudited)
(In thousands of U.S. dollars)

	Nine Months Ended September 30,	
	2022	**2021**
Operating activities		
Net loss	$ (44,112)	$ (45,525)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	6,789	8,548
Depreciation and amortization	1,193	916
Amortization of operating lease right-of-use assets	776	730
Amortization and accretion of premiums/discounts on available-for-sale securities	(105)	—
Loss on disposal of property and equipment	108	—
Changes in operating assets and liabilities:		
Other current assets and other non-current assets	(287)	36
Accounts payable and accrued liabilities	1,823	332
Operating lease liabilities	(859)	(427)
Net cash used in operating activities	(34,674)	(35,390)
Investing activities		
Purchases of property and equipment	(1,006)	(2,867)
Purchases of available-for-sale securities	(81,595)	—
Proceeds from maturities of available-for-sale securities	15,000	—
Net cash used in investing activities	(67,601)	(2,867)
Financing activities		
Proceeds from exercise of stock options	134	408
Payment on finance lease obligations	(54)	(2)
Proceeds from the issuance of common stock under Employee Stock Purchase Plan	63	219
Net cash provided by financing activities	143	625
Net change in cash, cash equivalents, and restricted cash during the period	(102,132)	(37,632)
Cash, cash equivalents, and restricted cash, beginning of period	143,345	193,434
Cash, cash equivalents, and restricted cash, end of period	$ 41,213	$ 155,802
Supplemental disclosure of non-cash investing and financing activities:		
Operating lease liabilities arising from obtaining ROU asset	$ —	$ 1,584
Purchases of property and equipment unpaid at period-end	$ 28	$ 297

The accompanying notes form an integral part of these condensed financial statements.

NEOLEUKIN THERAPEUTICS, INC.

Condensed Statements of Stockholders' Equity
(Unaudited)
(In thousands of U.S. dollars, except share amounts)

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Number	Amount	Capital	Income (Loss)	Deficit	Equity
Balances, December 31, 2021	42,457,471	$ —	$ 536,362	$ —	$ (393,498)	$ 142,864
Shares issued upon exercises of stock options	36,500	—	134	—	—	134
Stock-based compensation	—	—	2,446	—	—	2,446
Net loss	—	—	—	—	(15,351)	(15,351)
Balances, March 31, 2022	42,493,971	$ —	$ 538,942	$ —	$ (408,849)	$ 130,093
Issuance of shares under Employee Stock Purchase Plan	75,881	—	63	—	—	63
Shares issued upon vesting of restricted stock units	10,000	—	—	—	—	—
Stock-based compensation	—	—	2,312	—	—	2,312
Unrealized loss on available-for-sale securities	—	—	—	(72)	—	(72)
Net loss	—	—	—	—	(15,688)	(15,688)
Balances, June 30, 2022	42,579,852	$ —	$ 541,317	$ (72)	$ (424,537)	$ 116,708
Shares issued upon vesting of restricted stock units	14,750	—	—	—	—	—
Stock-based compensation	—	—	2,031	—	—	2,031
Unrealized loss on available-for-sale securities	—	—	—	(20)	—	(20)
Net loss	—	—	—	—	(13,072)	(13,072)
Balances, September 30, 2022	42,594,602	$ —	$ 543,348	$ (92)	$ (437,609)	$ 105,647

The accompanying notes form an integral part of these condensed financial statements.

NEOLEUKIN THERAPEUTICS, INC.

Condensed Statements of Stockholders' Equity
(Unaudited)
(In thousands of U.S. dollars, except share amounts)

	Common Stock		Additional Paid-In	Accumulated other comprehensive	Accumulated	Total Stockholders'
	Number	Amount	Capital	income (loss)	Deficit	Equity
Balances, December 31, 2020	42,196,296	$ —	$ 524,022	$ —	$ (332,806)	$ 191,216
Shares issued upon exercises of stock options	91,737	—	282	—	—	282
Shares issued upon vesting of restricted stock units	38,000	—	—	—	—	—
Stock-based compensation	—	—	2,420	—	—	2,420
Net loss	—	—	—	—	(14,950)	(14,950)
Balances, March 31, 2021	42,326,033	$ —	$ 526,724	$ —	$ (347,756)	$ 178,968
Shares issued upon exercises of stock options	25,124	—	95	—	—	95
Issuance of shares under Employee Stock Purchase Plan	22,972	—	219	—	—	219
Shares issued upon vesting of restricted stock units	45,000	—	—	—	—	—
Stock-based compensation	—	—	2,918	—	—	2,918
Net loss	—	—	—	—	(15,129)	(15,129)
Balances, June 30, 2021	42,419,129	$ —	$ 529,956	$ —	$ (362,885)	$ 167,071
Shares issued upon exercises of stock options	7,505	—	31	—	—	31
Shares issued upon vesting of restricted stock units	1,500	—	—	—	—	—
Stock-based compensation	—	—	3,210	—	—	3,210
Net loss	—	—	—	—	(15,446)	(15,446)
Balances, September 30, 2021	42,428,134	$ —	$ 533,197	$ —	$ (378,331)	$ 154,866

The accompanying notes form an integral part of these condensed financial statements.

NEOLEUKIN THERAPEUTICS, INC.

Notes to the Condensed Financial Statements
(Unaudited)

1. Nature of operations

Neoleukin Therapeutics, Inc. (“Neoleukin” or “the Company”) is a biopharmaceutical company creating next generation immunotherapies for cancer, inflammation, and autoimmunity using *de novo* protein design technology. Neoleukin uses sophisticated computational methods to design proteins that demonstrate specific pharmaceutical properties that provide potentially superior therapeutic benefit over native proteins.

2. Summary of significant accounting policies

(a) Basis of presentation

The accompanying unaudited condensed financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (“U.S. GAAP”) and pursuant to the rules and regulations of the United States Securities and Exchange Commission (“SEC”) for interim financial information. Accordingly, these financial statements do not include all of the information and footnotes required by U.S. GAAP for complete financial statements and should be read in conjunction with the audited consolidated financial statements and accompanying notes included in the Company’s Annual Report on Form 10-K for the year ended December 31, 2021, filed with the Securities and Exchange Commission on March 1, 2022.

In management’s opinion, the unaudited condensed financial statements reflect all adjustments (consisting of normal recurring adjustments) necessary to present fairly the financial position of the Company as of September 30, 2022, and results of operations and cash flows for all periods presented. The interim results presented are not necessarily indicative of results that can be expected for the full year ending December 31, 2022.The Company reclassified prior year interest income in the condensed statements of operations and comprehensive income (loss) to conform to current year presentation. This reclassification had no effect on net loss or comprehensive loss.

(b) Use of estimates and assumptions

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Significant areas requiring estimates include valuation and recognition of stock-based compensation, the incremental borrowing rate utilized in the measurement of operating and finance lease liabilities, amortization and depreciation of property, plant and equipment, and pre-clinical, clinical, and other accruals. Actual results could differ from those estimates.

(c) Leases

At contract inception, the Company determines if the contract is or contains a lease. Lease liabilities are recognized on the lease commencement date based on the estimated present value of lease payments over the lease term. To determine the present value of the lease payments, the Company utilizes its estimated incremental borrowing rate based on information available at the lease commencement date as the interest rate implicit in the lease is typically not readily determinable. The related right-of-use assets are recorded net of any lease incentives received. Variable lease cost primarily includes building operating expenses as charged to the Company by its landlords and payments for lessor-owned assets that are not covered by a tenant improvement allowance.

The Company includes options to extend the lease in its lease liability and right-of-use asset when it is reasonably certain that it will exercise that option. None of the Company's options to extend the rental term of any of its existing leases were considered reasonably certain as of September 30, 2022.

For leases of office space and equipment, the Company has elected to not separate the lease components from the non-lease components.

For leases with a lease term of 12 months or less and which do not include an option to purchase the underlying asset, the Company has elected to recognize the lease payments in the statement of operations on a straight-line basis over the lease term.

(d) Fair value of financial instruments

The carrying amounts of certain of the Company's financial instruments, including cash and cash equivalents, restricted cash, receivables, accounts payable and accrued liabilities, approximate their fair values because of their nature and/or short maturities.

Certain of the Company's financial instruments are measured at fair value on a recurring basis. The Company determines the fair value of those financial instruments based upon the fair value hierarchy, which prioritizes valuation inputs based on the observable nature of those inputs. The three levels of the fair value hierarchy are as follows:

Level 1 - quoted prices (unadjusted) in active markets for identical assets or liabilities that can be accessed on the measurement date
Level 2 - quoted prices (in non-active markets or in active markets for similar assets or liabilities), observable inputs other than quoted prices and inputs that are not directly observable but are corroborated by observable market data
Level 3 - unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities

At September 30, 2022 and December 31, 2021, the Company had $39.7 million and $140.9 million in money market funds, respectively. Money market funds and short-term investments, consisting entirely of investments in U.S. treasury securities, are Level 1 financial instruments as they are valued at the closing price reported by the fund sponsor from an actively traded exchange.

The following table presents information about the Company's financial instruments that are measured at fair value on a recurring basis:

	September 30, 2022			
(in thousands)	**Total**	**Level 1**	**Level 2**	**Level 3**
Financial assets				
Cash equivalents	$ 39,684	$ 39,684	$ —	$ —
Short-term investments	66,543	66,543	—	—
Total financial assets	$ 106,227	$ 106,227	$ —	$ —

	December 31, 2021			
(in thousands)	**Total**	**Level 1**	**Level 2**	**Level 3**
Financial assets				
Cash equivalents	$ 140,856	$ 140,856	$ —	$ —
Short-term investments	—	—	—	—
Total financial assets	$ 140,856	$ 140,856	$ —	$ —

(e) Investments

The Company's short-term investments consist entirely of investments in U.S. treasury securities. These investments are classified as available-for-sale debt securities and are therefore reported at fair value in the condensed balance sheets. Unrealized gains and losses are included in accumulated other comprehensive income (loss). There were no realized gains or losses on investments for the three and nine months ended September 30, 2022 and 2021.

The Company assesses investments for impairment at each reporting period. An investment is considered impaired when the amortized cost basis exceeds the fair value. When this is the case, the Company assesses whether the impairment is credit-related or noncredit-related based on various factors. When an impairment, or a portion of an impairment, is considered credit-related, an allowance for credit losses is recorded. For the nine months ended September 30, 2022, the Company recognized no year-to-date credit losses and no allowance for credit losses is

recorded as of September 30, 2022. The aggregate fair value of investments with unrealized losses as of September 30, 2022 is $66.5 million.

(f) Net loss per share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding for the period, without consideration for common stock equivalents. Common stock equivalents are included in the calculation of diluted earnings per share only in periods of net income and are excluded in the calculation of diluted net loss per share in periods of net loss as their inclusion would be anti-dilutive. Outstanding pre-funded warrants as of September 30, 2022 and September 30, 2021 are 12,663,010 and are considered outstanding as of their issuance date and are included in basic and diluted net loss per share because they are fully vested and exercisable for nominal cash consideration.

(g) Accounting for stock-based compensation

The Company has issued stock options and restricted stock units (“RSUs”). The Company measures the cost of services received in exchange for an award of equity instruments based on the grant-date fair value of the award. The cost of such award is recognized on a straight-line basis over the requisite service period, which is generally the vesting period. The Company accounts for forfeitures as they occur. The Company utilizes newly issued shares to satisfy option exercises, the vesting of RSUs, and 2020 Employee Stock Purchase Plan ("2020 ESPP") purchases.

The Company estimates the fair value of options using the Black-Scholes option pricing model on the grant date. This approximation uses assumptions regarding a number of inputs that requires management to make significant estimates and judgments. The expected term represents the period that the Company’s stock-based awards are expected to be outstanding. As the Company does not have sufficient historical experience for determining the expected term of the stock option awards granted, the Company has based its expected term for awards issued to employees on the simplified method, which represents the average period from vesting to the expiration of the stock option. In addition, the Company does not have sufficient trading history of the Company’s common stock, and therefore, the expected stock price volatility for the Company’s common stock was estimated by taking the average historical price volatility for industry peers. The Company has never declared or paid any cash dividends to common stockholders and does not presently plan to pay cash dividends in the foreseeable future. Consequently, the Company used an expected dividend yield of zero. The risk-free interest rate was based on the yields of treasury securities with maturities similar to the expected term of the options for each option group.

The fair value of each RSU is measured using the closing price of the Company’s common stock on the date of grant.

(h) Recently issued and recently adopted accounting standards

In June 2016, the FASB issued Accounting Standard Update ("ASU") No. 2016-13, Measurement of Credit Losses on Financial Instruments (ASU 2016-13), which replaces the incurred loss impairment methodology under current GAAP with a methodology that reflects expected credit losses and requires consideration of a broader range of reasonable and supportable information to inform credit loss estimates. In November 2019, the FASB issued ASU 2019-10, Financial Instruments – Credit Losses (Topic 326), Derivatives (Topic 815), and Leases (Topic 842). This ASU delayed the required adoption for SEC filers that are smaller reporting companies as of their determination on November 15, 2019, until annual and interim periods beginning after December 15, 2022, with early adoption permitted. The Company adopted this standard in conjunction with the investment in debt securities during the quarter ended June 30, 2022.

3. Cash, cash equivalents, and restricted cash

The Company considers all highly liquid investments with an original contractual maturity or a remaining maturity of three months or less at the date of purchase to be cash equivalents. Cash equivalents as of September 30, 2022 and December 31, 2021 consisted of money market funds.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash in the condensed balance sheets that sum to the total of the same such amounts shown in the condensed statements of cash flows:

(in thousands)	September 30, 2022	December 31, 2021
Cash and cash equivalents	$ 40,335	$ 142,467
Restricted cash	878	878
Total cash, cash equivalents, and restricted cash	$ 41,213	$ 143,345

Restricted cash, included in other non-current assets in the condensed balance sheets, includes $0.9 million in cash deposits the Company maintains with its bank as collateral for the irrevocable letters of credit related to its lease obligations.

4. Investments

The Company's investments consist of the following:

	September 30, 2022			
(in thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities - due within 1 year	$ 66,635	$ —	$ (92)	$ 66,543
Money market funds	39,684	—	—	39,684
Total	$ 106,319	$ —	$ (92)	$ 106,227

	December 31, 2021			
(in thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities - due within 1 year	$ —	$ —	$ —	$ —
Money market funds	140,856	—	—	140,856
Total	$ 140,856	$ —	$ —	$ 140,856

5. Leases

The Company enters into lease arrangements for its facilities as well as certain equipment, classified either as operating or finance leases.

The Company has an operating lease agreement, as amended by the execution of two subsequent amendments, for approximately 33,300 square feet of office space in Seattle, Washington for the Company’s principal executive offices, a laboratory for research and development, and related uses. The lease commenced on January 15, 2020 and expires on February 1, 2029, with the option to extend the lease for two five-year terms. The lease provides for a tenant improvement allowance of up to $9.5 million, which has been fully utilized.

The Company has an operating lease agreement for approximately 6,272 square feet of office space in Seattle, Washington, for additional office and laboratory space for research and development and related uses. In March 2021, the Company executed an amendment to this lease pursuant to which the contractual lease term was extended through September 30, 2026, unless terminated earlier, with the option to extend the lease for an additional 28-month term. The execution of this amendment was accounted for as a modification to the lease due to the extension of the lease term and an increase in lease payments, and the Company recorded an increase in the lease liability and related right-of-use asset of $1.6 million.

As of September 30, 2022, and December 31, 2021, the Company's operating lease right-of-use assets were $10.0 million and $10.8 million, respectively. As of September 30, 2022, and December 31, 2021, the Company's finance lease right-of-use assets, included within property and equipment on the condensed balance sheets, were $0.2 million and $0.2 million, respectively.

6. Equity

(a) Common stock and pre-funded warrants

The Company is authorized to issue 100,000,000 shares of common stock with a par value of $0.000001 as of September 30, 2022 and December 31, 2021. As of September 30, 2022 and December 31, 2021, the total number of shares of common stock issued and outstanding was 42,594,602 and 42,457,471, respectively.

As of September 30, 2022, the Company had pre-funded warrants outstanding to purchase an aggregate of 12,663,010 shares of common stock. The pre-funded warrants are exercisable at any time for an exercise price of $0.000001, except that the pre-funded warrants cannot be exercised by the holders if, after giving effect thereto, the holders would beneficially own more than 9.99% of the outstanding common stock, subject to certain exceptions. However, any holder may increase or decrease such percentage to any other percentage (not in excess of 19.99%) upon at least 61 days' prior notice from the holder to the Company. The holders of the pre-funded warrants will not have the right to vote on any matter except to the extent required by Delaware law.

On November 4, 2021, the Company entered into an ATM or "at-the-market" Equity Offering Sales Agreement (the "Sales Agreement") with BofA Securities, Inc., as agent ("BofA"), pursuant to which the Company may offer and sell, from time to time through BofA, shares of the Company's common stock, having an aggregate offering price of up to $40.0 million. The offer and sale of the shares will be made pursuant to a shelf registration statement on Form S-3 and the related prospectus filed on December 11, 2020, and declared effective by the SEC on December 21, 2020, as supplemented by a prospectus supplement dated November 4, 2021. The Company has no obligation to sell any such shares under the Sales Agreement. Through September 30, 2022, no sales of common stock have been made pursuant to the Sales Agreement.

(b) Stock-based compensation expense

Stock-based compensation expense is classified in the condensed statements of operations as follows:

(in thousands)	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Research and development expenses	$ 973	$ 1,423	$ 3,288	$ 3,850
General and administrative expenses	1,058	1,787	3,501	4,698
Total stock-based compensation expense	$ 2,031	$ 3,210	$ 6,789	$ 8,548

Total unrecognized compensation expense for all stock-based compensation plans was $17.8 million as of September 30, 2022. This expense is expected to be recognized over a weighted average remaining vesting period of 2.33 years.

The fair values of stock options granted are estimated using the Black-Scholes option pricing model with the following weighted average assumptions:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Expected volatility	84.18 %	89.17 %	83.80 %	89.18 %
Expected dividends	0 %	0 %	0 %	0 %
Expected terms (years)	6.08	6.07	6.04	6.03
Risk free rate	2.83 %	0.83 %	2.63 %	0.89 %

(c) Stock options

A summary of the Company's stock option activity and related information for the nine months ended September 30, 2022 is as follows:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (in Years)	Aggregate Intrinsic Value (in Thousands)
Outstanding at December 31, 2021	8,963,945	$ 7.20	8.32	$ 6,912
Options granted	3,360,450	$ 1.34		
Options exercised	(36,500)	$ 3.67		
Options cancelled/forfeited	(2,871,996)	$ 7.86		
Outstanding at September 30, 2022	9,415,899	$ 4.92	8.30	$ —
Exercisable as of September 30, 2022	3,729,902	$ 6.04	7.16	$ —

During the nine months ended September 30, 2022, 36,500 shares of common stock were issued upon exercise of options with an aggregate intrinsic value of $0.1 million. During the nine months ended September 30, 2021, 124,366 shares of common stock were issued upon exercise of options with an aggregate intrinsic value of $1.3 million. The weighted-average grant date fair value of options granted during the nine months ended September 30, 2022 and September 30, 2021 was $0.96 and $6.49 per share, respectively.

(d) Restricted stock units

A summary of the Company's RSU activity and related information for the nine months ended September 30, 2022 is as follows:

	Number of Shares	Weighted Average Grant Date Fair Value
Non-vested at December 31, 2021	132,000	$ 9.97
Restricted stock units granted	700,000	$ 3.69
Restricted stock units vested	(24,750)	$ 12.20
Restricted stock units forfeited	(353,000)	$ 4.86
Non-vested at September 30, 2022	454,250	$ 4.14

(e) Employee stock purchase plan

The Company's 2020 ESPP was adopted by the Company's Board of Directors in March 2020 and approved by the Company's stockholders in May 2020. A total of 759,936 shares of common stock have been reserved for issuance under the 2020 ESPP.

Subject to share and dollar limits as described in the plan, the 2020 ESPP allows eligible employees to contribute, through payroll deductions, up to 15% of their earnings for the purchase of shares of the Company's common stock at the lower of 85% of the closing price of the Company's common stock on the first trading day of the offering period or 85% of the closing price of the Company's common stock on the last trading day of the offering period. There are two six-month offering periods during each fiscal year, ending on May 15 and November 15.

For the nine months ended September 30, 2022, the Company issued 75,881 shares of common stock at a purchase price of $0.83 per share under the 2020 ESPP. Cash received from the purchases under the 2020 ESPP for the nine months ended September 30, 2022 was $0.1 million. As of September 30, 2022, $0.1 million of employee contributions are included in accounts payable and accrued liabilities in the accompanying condensed balance sheet.

7. Net loss per share

The Company excluded the following potentially dilutive shares from diluted net loss per share as the effect would have been anti-dilutive for all periods presented:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Outstanding stock options	9,415,899	9,619,138	9,415,899	9,619,138
Restricted stock units	454,250	170,500	454,250	170,500
Shares issuable under 2020 ESPP	61,922	24,965	61,922	24,965
	9,932,071	9,814,603	9,932,071	9,814,603

8. Subsequent events

Effective November 12, 2022, the Company's Board of Directors approved a strategic decision to discontinue further development of NL-201, and to move forward focusing the Company's investment in early stage pre-clinical development of the next generation of *de novo* proteins. The Board of Directors also approved a restructuring plan, including a reduction in force of approximately 40%. The Company's current best estimate of costs it will incur total between $6.3 million and $8.3 million, consisting of severance, benefits, costs associated with the discontinuation of further development of NL-201, and other costs. The majority of these costs are expected to be incurred during the fourth calendar quarter of 2022 and the first half of 2023, and the Company expects the execution of the restructuring plan will be substantially complete by the second calendar quarter of 2023.

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

You should read the following discussion of our financial condition and results of operations in conjunction with the unaudited interim condensed financial statements and notes thereto included elsewhere in this report and our audited consolidated financial statements and notes included as part of our Annual Report on Form 10-K for the year ended December 31, 2021.

Forward-Looking Statements

The following discussion of our financial condition and results of operations contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. All statements other than statements of historical facts are "forward-looking statements" for purposes of these provisions, including those relating to future events or our future financial performance and financial guidance. In some cases, you can identify forward-looking statements by terminology such as "may," "might," "will," "should," "expect," "plan," "anticipate," "project," "believe," "estimate," "predict," "potential," "intend" or "continue," the negative of terms like these or other comparable terminology, and other words or terms of similar meaning in connection with any discussion of future operating or financial performance. These statements are only predictions. All forward-looking statements included in this document are based on information available to us on the date hereof, and we assume no obligation to update any such forward-looking statements. Any or all of our forward-looking statements in this document may turn out to be wrong. Actual events or results may differ materially. Our forward-looking statements can be affected by inaccurate assumptions we might make or by known or unknown risks, uncertainties and other factors. In evaluating these statements, you should specifically consider various factors, including the risks outlined under the caption "Risk Factors" set forth in Item 1A of Part II of this quarterly report on Form 10-Q, as well as those contained from time to time in our other filings with the SEC. We caution investors that our business and financial performance are subject to substantial risks and uncertainties.

Overview

We are a biopharmaceutical company creating next generation immunotherapies for cancer, inflammation, and autoimmunity using *de novo* protein design technology. We use sophisticated computational methods to design proteins that demonstrate specific pharmaceutical properties that provide potentially superior therapeutic benefit over native proteins. Protein engineering methods generally involve the modification of native proteins. With our *de novo* protein design process we design new protein scaffolds from the ground up, capable of demonstrating specific biological properties. Through this method we are able to produce proteins that, while resembling native proteins, may have novel molecular interfaces, differential activation of specific cell types, increased stability, or improved biodistribution compared to native proteins in order to deliver greater therapeutic benefit. With the introduction of machine learning to this process in recent months, we have been able to accelerate our timeline for adding potential candidates in our pipeline. *De novo* proteins have the capacity to be cytokine receptor agonists, antagonists, or result in conditional activation of specific cytokine receptors such that they may regulate inflammation or the immune response to cancer and inflammatory conditions. To date, we have been focused on key cytokine mimetics, which we refer to as Neoleukin *de novo* cytokine mimetics. Neoleukin d*e novo* cytokine mimetics can be modified to adjust affinity, thermodynamic stability, resistance to biochemical modification, pharmacokinetic characteristics, potency and targeting to tumor or inflamed tissues.

On August 8, 2019, Neoleukin Therapeutics, Inc. ("Former Neoleukin"), completed its merger with Aquinox, in accordance with the terms of the Agreement and Plan of Merger dated August 5, 2019 ("Merger Agreement"), by and among Aquinox, Former Neoleukin and Apollo Sub, Inc., a wholly-owned subsidiary of Aquinox. Pursuant to the Merger Agreement, Apollo Sub, Inc. merged with and into Former Neoleukin, with Former Neoleukin surviving the merger as a wholly-owned subsidiary of Aquinox (the "Merger"). Upon completion of the Merger, Aquinox was renamed Neoleukin Therapeutics, Inc. and Former Neoleukin was renamed Neoleukin Corporation. On July 31, 2020, we sold all issued and outstanding capital stock of our Canadian subsidiary, Aquinox Pharmaceuticals (Canada) Inc. to an unrelated third party. On December 31, 2020, Neoleukin Corporation was merged into Neoleukin Therapeutics, Inc.

Recent Developments

On November 12, 2022, we made a strategic decision to focus our resources on the next generation of immunotherapies using *de novo* protein design, advanced machine learning, and the lessons we have learned from our development of *de novo* cytokine mimetics, including NL-201. Moving forward, we expect to focus on technology that widens the therapeutic window, such as the development of targeted and conditionally activated molecules to create potent immune agonists. We believe we are well positioned to do this work based on our expertise in *de novo* protein design combined with our experience in advanced machine learning and neural networks, which allows us to predict and create structures for *de novo* proteins with more sophisticated and dynamic structural elements than was previously possible.

This shift in focus coincides with our strategic decision to discontinue development for our lead product candidate, NL-201. We believe NL-201 was the first fully *de novo* protein to be evaluated in clinical trials, and during the monotherapy arm of the trial, we were able to demonstrate engagement of the target receptor and expected pharmacodynamic changes for a potent IL-2/IL-15 agonist. Furthermore, our preliminary monotherapy data does not demonstrate significant immunogenicity even after multiple cycles of therapy, which is an important de-risking of the potential for *de novo* proteins. However, based on a review of the preliminary data, the expected benefit to risk ratio for patients, and recent developments in the field of IL-2 therapeutics, we determined that the resources required to continue development would be better applied to advancing the next generation of *de novo* protein therapeutics.

As a result of the decision to discontinue development of NL-201, on November 12, 2022, our Board of Directors approved a restructuring plan, including a reduction in force of approximately 40%. Cost savings as a result of this reduction in force as well as the discontinuation of development of NL-201 are expected to extend our existing cash runway into the second half of 2025.

NL-201

NL-201 is an IL-2/IL-15 agonist designed to eliminate binding to the alpha subunit of the IL-2 receptor (also known as CD25) while enhancing binding to the beta and gamma subunits, We elected to take NL-201 into clinical trial initially because of the potential for differentiation from IL-2 demonstrated in initial research. In multiple preclinical animal models, a precursor to NL-201 demonstrated substantial anti-tumor activity without detectable binding to CD25, as compared to native IL-2. Following these preclinical studies, we further refined our precursor to extend its half-life, resulting in the NL-201 product candidate. We then completed multi-dose, non-GLP and GLP toxicology studies of NL-201 in rats and non-human primates, and initiated our first in-human clinical trial. This included completion of GLP in-life dosing with no unexpected toxicities observed. NL-201 was intended to be used as either a single-agent or in combination with complementary therapeutic modalities, including checkpoint inhibitors, and may also hold promise as a therapeutic to be used in combination with allogeneic cellular therapies to expand and maintain populations of transplanted CAR-T and natural killer ("NK") cells.

Recombinant human IL-2 (rhIL-2) is one of the few immuno-oncology drugs with demonstrated activity as a single agent. IL-2 has a confirmed mechanism of action for treating tumors; however, it has encountered issues as a therapeutic due to the preferential binding and activation of cells that contain CD25, the alpha subunit of the heterotrimeric IL-2 receptor. CD25 induces conformational changes in IL-2 that enable high-affinity binding to the beta and gamma subunits of the IL-2 receptor. At high doses, preferential binding to endothelial cells expressing CD25 is believed to exacerbate vascular leak syndrome, whereas at low doses, preferential activation of CD25-expressing regulatory T cells (Tregs) can inhibit anticancer immune responses. Due to IL-2's potential for severe toxicity, with vascular leak syndrome and cytokine storm being frequent side effects, and reduced efficacy over time, its use as a therapeutic has been limited. Further, low-dose treatment with IL-2 has generally been insufficient to demonstrate antitumor activity.

While the problem posed by IL-2 is well understood, it has been difficult to modify native IL-2 to retain potent activation of IL-2 receptor while eliminating binding to CD25. Instead of modifying native IL-2, NL-201 was developed using computational methods to design a new sequence with the proper intermolecular interactions to efficiently bind the beta and gamma subunits while eliminating CD25 binding. As opposed to traditional recombinant protein therapeutics, *de novo* proteins are entirely novel sequences with limited homology to native proteins. While there is a potential that patients may mount an anti-drug immune response against NL-201, we believe that this risk may be mitigated by several factors, including the stability of the protein and its resistance to proteolytic degradation.

In May 2021, we enrolled the first patient in a Phase 1 clinical trial of NL-201 for advanced solid tumors. On May 16, 2022, we announced that we had begun dosing patients in a new arm of the clinical trial study with a combination of NL-201 and Merck's checkpoint inhibitor KEYTRUDA® (pembrolizumab). On November 12, 2022, we made the decision to discontinue development of NL-201 for strategic reasons and focus our resources on advancing the next generation of *de novo* protein therapeutics, using the lessons we have learned from our development of NL-201. We have also discontinued plans for any future trials, including a Phase 1 clinical trial in hematological malignancies.

Other Research Programs

Beyond our initial focus on NL-201, our research team is using *de novo* protein design to develop additional molecules as therapeutic candidates. In 2020, we reported development of NL-CVX1, a fully *de novo* decoy protein that was designed to block infection of human cells by the SARS-CoV-2 virus. In June 2021, we suspended plans to develop this molecule as effective vaccines became widely available; however, we believe this is a powerful example of the capability of our technology to develop potential *de novo* therapies in a short time frame. In 2021, we reported preclinical data for an inhibitor of IL-2 and IL-15 activity, Neo-5171, which demonstrated in vivo anti-inflammatory activity. In 2022, we announced that we are exploring a targeted activator of T-regulatory cells for the treatment of inflammation and autoimmune diseases.

Recently, our scientists have been incorporating machine learning and neural networks to our existing *de novo* protein design methods to more quickly develop potential therapeutics that we believe will be able to address significant unmet medical needs in areas including oncology, inflammation, and autoimmunity. Advances in machine learning, combined with the expertise and experience of our protein design and research team, expands the scope of our *de novo* protein design process to include complex structures.

Following the decision to discontinue development of NL-201, we are focused on research into the next generation of *de novo* cytokine mimetics that widen the therapeutic window, such as the development of targeted and conditionally activated molecules to create potent immune agonists. We expect to combine our expertise in *de novo* protein design, including data gathered from the development of NL-201 and research into other novel cytokine mimetics, with advances in machine learning and neural networks to create more sophisticated and dynamic structural elements than was previously possible. Additional candidates will enter our preclinical pipeline as they become validated.

Finances

We will need to raise substantial additional capital to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we plan to finance our operations through the sale of equity, debt financings, or other capital sources, which may include collaborations with other companies or other strategic transactions. There are no assurances that we will be successful in obtaining an adequate level of financing as and when needed to finance our operations on terms acceptable to us or at all. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to secure adequate additional funding, we may have to significantly delay, scale back, or discontinue the development and commercialization of one or more product candidates, reduce our early stage research projects, reduce the size of our team, or delay our pursuit of potential in-licenses or acquisitions.

Based upon our current operating plan, we believe our cash-on-hand will be sufficient to fund operations into the second half of 2025.

COVID-19 Impact

The COVID-19 pandemic has impacted worldwide economic activity during a time of extremely elevated health risks that necessitated a move away from business as usual. During this unprecedented time, protecting the health and well-being of our employees and community was a top priority, which we had to balance against trying to maintain continuity of our research, development, and business activities. Our industry, along with many others, has also experienced supply chain disruptions related to the COVID-19 pandemic that impacted our ability to do business as usual and increased certain costs of doing business.

In March 2020, we transitioned to a work from home policy for our employees and discontinued all work-related travel. Beginning in the first quarter of 2021, our offices reopened, with some employees returning to working in person in accordance with guidance from Washington State and the U.S. Centers for Disease Control and Prevention ("CDC") and applicable regulations. As of the end of the third quarter of 2022, we have returned essentially all of our employees to in-office work with hybrid schedules, and have resumed travel to in-person conferences and events, although we continue to assess the ongoing impacts of the COVID-19 pandemic on our workforce, supply chain, and availability of critical vendors. We have been able to continue our business-critical research and development work throughout the pandemic, adhering to employee safety guidelines. As we move forward, we will continue to assess our work policies and monitor federal, state, and local guidance and regulations to determine any changes to work practices that may be necessary in the event of any resurgence of the COVID-19 pandemic.

Results of Operations

Operating Expenses

The following table summarizes our operating expenses for the three and nine months ended September 30, 2022 and 2021:

	Three Months Ended September 30,		Change		Nine Months Ended September 30,		Change	
(in thousands)	**2022**	**2021**	**$**	**%**	**2022**	**2021**	**$**	**%**
Research and development	$ 9,471	$ 9,896	$ (425)	(4)%	$ 31,128	$ 29,402	$ 1,726	6 %
General and administrative	4,138	5,556	(1,418)	(26)%	13,718	16,122	(2,404)	(15)%
Total operating expenses	$ 13,609	$ 15,452	$ (1,843)	(12)%	$ 44,846	$ 45,524	$ (678)	(1)%

Research and Development Expenses

Research and development expenses consist primarily of costs incurred under arrangements with third parties, such as contract research organizations ("CROs"), manufacturing organizations, and consultants, personnel-related costs (including stock-based compensation and travel expenses), facility-related costs, and lab supplies.

For the three months ended September 30, 2022, research and development expenses were $9.5 million, compared to $9.9 million for the three months ended September 30, 2021. The decrease in research and development expenses during the three months ended September 30, 2022 is primarily due to a decrease in personnel-related costs, offset partially by increases in costs related to our Phase 1 clinical trial of NL-201.

For the nine months ended September 30, 2022, research and development expenses were $31.1 million, compared to $29.4 million for the nine months ended September 30, 2021. The increase in research and development expenses during the nine months ended September 30, 2022 is due to increases in costs related to our Phase 1 clinical trial of NL-201, offset partially by a decrease in personnel-related costs and a decrease in NL-CVX1 costs due to the suspension of this program in June 2021.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel-related costs (including stock-based compensation and travel expenses), facility-related costs, insurance, and professional fees for consulting, legal, and accounting services.

For the three months ended September 30, 2022, general and administrative expenses were $4.1 million, compared to $5.6 million for the three months ended September 30, 2021. The decrease in general and administrative expenses during the three months ended September 30, 2022 was primarily due to a decrease in personnel-related costs.

For the nine months ended September 30, 2022, general and administrative expenses were $13.7 million, compared to $16.1 million for the nine months ended September 30, 2021. The decrease in general and administrative expenses during the nine months ended September 30, 2022 was primarily due to decreases in personnel-related and facility-related costs.

Other income (loss), net

(in thousands)	Three Months Ended September 30, 2022	2021	Change $	Change %	Nine Months Ended September 30, 2022	2021	Change $	Change %
Interest income	$ 559	$ 6	$ 553	*	$ 766	$ 14	$ 752	*
Foreign exchange gains/(losses)	1	—	1	*	8	(3)	11	*
Other expenses	(23)	—	(23)	*	(40)	(12)	(28)	*
Total other income (loss), net	$ 537	$ 6	$ 531	*	$ 734	$ (1)	$ 735	*

**Not meaningful*

The increase in interest income during the three and nine months ended September 30, 2022, as compared to the three and nine months ended September 30, 2021, was due to broad increases in the interest rate environment resulting in higher interest earned on our money market fund investments. Additionally, the increase is due to purchases of U.S. treasury securities during 2022 which yield a higher rate of interest than investments in money market funds.

Liquidity and Capital Resources

Since our inception, we have incurred net losses and negative cash flows from our operations. Our operating activities used $34.7 million and $35.4 million of cash flows during the nine months ended September 30, 2022 and 2021, respectively. As of September 30, 2022, we had an accumulated deficit of $437.6 million, working capital of $98.6 million, and cash, cash equivalents, and short-term investments of $106.9 million.

On November 4, 2021, we entered into an ATM "at-the-market" Equity Offering Sales Agreement, or the Sales Agreement, with BofA Securities, Inc., or BofA, pursuant to which we may, but are not obligated to, offer and sell, from time to time, shares of our common stock with an aggregate offering price up to $40.0 million through BofA, as sales agent. No sales of our common stock have been made pursuant to this Sales Agreement to date.

Cash Flows

The following table summarizes our cash flows for the nine months ended September 30, 2022 and 2021:

(in thousands)	Nine Months Ended September 30, 2022	2021
Net cash (used in) provided by:		
Operating activities	$ (34,674)	$ (35,390)
Investing activities	(67,601)	(2,867)
Financing activities	143	625
Net change in cash, cash equivalents, and restricted cash	$ (102,132)	$ (37,632)

Net cash used in operating activities

Net cash used in operating activities for the nine months ended September 30, 2022 and September 30, 2021 consisted of net loss for the period adjusted for non-cash items and changes in components of operating assets and liabilities. For the nine months ended September 30, 2022, a net loss of $44.1 million was adjusted for non-cash items including stock-based compensation expense of $8.8 million and a net decrease of $0.7 million due to changes in operating assets and liabilities. For the nine months ended September 30, 2021, a net loss of $45.5 million was adjusted for non-cash items including stock-based compensation expense of $8.5 million and a net decrease of $0.1 million due to changes in operating assets and liabilities.

Net cash used in investing activities

For the nine months ended September 30, 2022, cash used in investing activities consisted primarily of purchases of available-for-sale securities and laboratory equipment. For the nine months ended September 30, 2021, cash used in investing activities consisted primarily of purchases of laboratory equipment and office furnishings.

Net cash provided by financing activities

For the nine months ended September 30, 2022 and September 30, 2021, net cash provided by financing activities consisted primarily of proceeds from stock option exercises and purchases of common stock under our 2020 Employee Stock Purchase Plan.

Operating and Capital Expenditure Requirements

We have not generated product revenue or achieved profitability since our inception and we expect to continue to incur net losses for the foreseeable future. As of September 30, 2022, we had approximately $106.9 million in cash, cash equivalents, and short-term investments. Based on our current business plans, we believe that our existing cash, cash equivalents, and short-term investments will be sufficient to fund our planned operations into the second half of 2025. However, our future capital requirements and the period for which we expect our existing resources to support our operations, fund expansion, develop new or enhanced products, or otherwise respond to competitive pressures, may vary significantly from our expectation and we may need to seek additional funds sooner than planned. Unless and until we generate sufficient revenue to be profitable, we will seek to fund our operations through public or private equity or debt financings or other sources. If we raise additional funds through the issuance of convertible debt securities, these securities could have rights senior to those of our common stock and could contain covenants that restrict our operations. There can be no assurance that we will be able to obtain additional equity or debt financing on terms acceptable to us, if at all. Our failure to obtain sufficient funds on acceptable terms when needed could have a negative impact on our business, results of operations, financial condition, cash flows, and future prospects. Our future capital requirements will depend on many factors, including:

- the number and characteristics of any future product candidates we develop or may acquire;
- the scope, progress, results, and costs of researching and developing our product candidates or any future product candidates, and conducting preclinical studies and clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals for any future product candidates;
- the cost of manufacturing our future product candidates and any products that may achieve regulatory approval;
- the cost of commercialization activities if any product candidates or future product candidates are approved for sale, including marketing, sales and distribution costs;
- the timing, receipt and amount of sales of, or royalties on, future approved products, if any;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of such agreements;
- any product liability or other lawsuits related to our products;
- the potential delays in our preclinical studies, our development programs and our planned clinical trials due to the continued impacts of the COVID-19 pandemic and related economic pressures, including supply chain disruptions, and other disruptions that may occur with any resurgence of acute cases of SARS-CoV-2, including resurgences relating to new variants;
- the expenses needed to attract and retain skilled personnel; and
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation.

Please see Item 1A of Part II of this Quarterly Report titled “Risk Factors” for additional risks associated with our substantial capital requirements.

Critical Accounting Policies and Significant Judgments and Estimates

The preparation of these financial statements in accordance with U.S. GAAP requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue, and expenses and the disclosure of contingent assets and liabilities in our financial statements. We evaluate our estimates and judgments on an ongoing basis. We base our estimates on historical experience, known trends and events, and various other factors that we believe 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. A summary of our significant accounting policies is presented in Part II, Item 8 of our Annual Report on Form 10-K for the year ended December 31, 2021. There have been no material changes to our significant accounting policies during the three and nine months ended September 30, 2022 other than those discussed in Note 2(g) in the Notes to Condensed Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q.

Recent Accounting Pronouncements

See Note 2(g), *Recently issued and recently adopted accounting standards* in the Notes to Condensed Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

As a “smaller reporting company,” as defined by Rule 12b-2 of the Exchange Act, and pursuant to Item 305 of Regulation S-K, we are not required to provide quantitative and qualitative disclosures about market risk.

Item 4. Controls and Procedures

Evaluation of disclosure controls and procedures. Under the supervision and with the participation of our principal executive and financial officer, our management conducted an evaluation 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 Exchange Act, as of the end of the period covered by this report.

In designing and evaluating our disclosure controls and procedures, management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply its judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Based on management’s evaluation, our principal executive and financial officer concluded that our disclosure controls and procedures are designed to, and are effective to, provide assurance at a reasonable level that the information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our principal executive and financial officer, as appropriate, to allow timely decisions regarding required disclosures.

Changes in internal control over financial reporting. There have not been any changes in our internal control over financial reporting during the quarter ended September 30, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Part II. Other Information

Item 1. Legal Proceedings

We may from time to time be named as a party to legal claims, actions and complaints, including matters involving employment, intellectual property or others. We are not presently a party to any legal proceedings that, in the opinion of our management, would reasonably be expected to have a material adverse effect on our business, financial condition, operating results or cash flows if determined adversely to us. Regardless of the 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

Summary of Risk Factors

An investment in our common stock involves various risks, and prospective investors are urged to carefully consider the matters discussed in the section titled “Risk Factors” prior to making an investment in our common stock. These risks include, but are not limited to, the following:

- We will require substantial additional capital to finance our operations which may not be available to us on acceptable terms, or at all. If we fail to obtain necessary financing, we may be unable to complete the development and potential commercialization of our product candidates.
- Our current stock price does not meet the listing requirements for the Nasdaq market on which our common stock is traded, and failure to meet listing requirements may result in a delisting of our stock from that exchange, which would adversely impact our ability to raise capital through future equity financings and decrease the value and liquidity of our common stock.
- We have incurred significant losses in every quarter since our inception and anticipate that we will continue to incur significant losses in the future.
- We have a limited operating history, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- We currently have no source of product revenue and may never become profitable.
- Our product candidates are in early stages of development and may fail in development or suffer delays that materially and adversely affect their commercial viability. If we are unable to complete development of, or commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.
- Our business is heavily dependent on the success of our Neoleukin *de novo* protein design technology. Existing and future preclinical studies and clinical trials of our product candidates may not be successful, and if we are unable to commercialize these product candidates or experience significant delays in doing so, our business will be materially harmed.
- Future clinical trials or additional preclinical studies may reveal significant adverse events not seen in our earlier preclinical studies and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our product candidates.
- If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.
- Our approach to the discovery and development of our therapeutic treatments is based on *de novo* protein design technology which is unproven and may not result in marketable products.
- We rely on and expect to continue to rely on third parties to conduct certain of our preclinical studies and clinical trials. If those third parties do not perform as contractually required, fail to satisfy legal or regulatory requirements, miss expected deadlines, or terminate the relationship, our development program could be delayed with potentially material and adverse effects on our business, financial condition, results of operations, and prospects.

- We rely on and expect to continue to rely on third-party manufacturers and suppliers to supply components of our product candidates. The loss of our third-party manufacturers or suppliers, or our or their failure to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, would materially and adversely affect our business.
- Unfavorable global economic conditions or other geopolitical developments could adversely affect our business, financial condition, stock price, and results of operations.
- If we are not able to obtain, maintain, and enforce patent protection and other intellectual property rights for our product candidates, our Neoleukin design process, or other proprietary technologies we may develop, and the development and commercialization of our product candidates may be adversely affected.

Risk Factors

You should carefully consider the following risk factors, in addition to the other information contained in this Quarterly Report on Form 10-Q, including our condensed financial statements and related notes. If any of the events described in the following risk factors occurs, our business, operating results, and financial condition could be adversely affected. This Quarterly Report on Form 10-Q also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this Quarterly Report on Form 10-Q.

Risks Related to Our Financial Position and Capital Needs

We will require substantial additional capital to finance our operations which may not be available to us on acceptable terms, or at all. If we fail to obtain necessary financing, we may be unable to complete the development and potential commercialization of our product candidates.

The development of biopharmaceutical product candidates is capital-intensive. If our product candidates enter and advance through preclinical studies and clinical trials, we will need substantial additional funds to expand or create our development, regulatory, manufacturing, marketing, and sales capabilities. We have used substantial funds to develop our technology and product candidates and will require significant funds to conduct further research and development and preclinical testing and clinical trials of our product candidates, to seek regulatory approvals for our product candidates, and to manufacture and market products, if any, which are approved for commercial sale. In addition, we expect to continue incurring costs associated with operating as a public company.

Preclinical studies and clinical trials for our product candidates will require substantial funds to complete. As of September 30, 2022, we had approximately $106.9 million in cash, cash equivalents, and short-term investments. We expect to incur substantial expenditures in the foreseeable future as we seek to advance future product candidates through preclinical and clinical development, the regulatory approval process and, if approved, commercial launch activities. In addition, we will incur costs related to the discontinued development of NL-201 in the near term. Based on our current operating plan, we believe that our available cash, cash equivalents, and short-term investments will be sufficient to fund our operating expenses and capital expenditure requirements into the second half of 2025. However, our future capital requirements and the period for which we expect our existing resources to support our operations, fund expansion, develop new or enhanced products, or otherwise respond to competitive pressures, may vary significantly from what we expect, and we may need to seek additional funds sooner than planned. Our monthly spending levels vary based on new and ongoing research and development and other corporate activities, and may also be impacted by inflationary pressures in the current economic environment. Because the length of time and activities associated with successful research and development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any marketing and commercialization activities for approved products. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the timing, cost and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- the progress of the development efforts of parties with whom we have entered or may in the future enter into collaborations and/or research and development agreements;

- the timing and amount of milestone and other payments we may receive or make under our collaboration agreements;
- our ability to maintain our current licenses and to establish new collaboration arrangements;
- the costs involved in prosecuting and enforcing patent and other intellectual property claims;
- the costs of manufacturing our product candidates by third parties;
- the cost of regulatory requirements, regulatory submissions and timing of regulatory approvals;
- the potential delays in our preclinical studies, our development programs and our ongoing and planned clinical trial activities due to the effects of global events, including macroeconomic conditions and continued supply chain disruptions;
- the impact of inflationary pressures on salaries and wages, and costs of goods and transportation expenses, among other things;
- the cost of commercialization activities if our product candidates or any future product candidates are approved for sale, including marketing, sales and distribution costs; and
- our efforts to enhance operational systems and hire additional personnel, including personnel to support development of our product candidates.

If we are unable to obtain funding on a timely basis or on acceptable terms, we may have to delay, reduce, or terminate our research and development programs and preclinical studies or future clinical trials, limit strategic opportunities, or undergo reductions in our workforce or other corporate restructuring activities. We do not expect to realize revenue from sales of commercial products or royalties from licensed products in the foreseeable future, if at all, and, in no event would we recognize such revenues, before our product candidates are clinically tested, approved for commercialization and successfully marketed.

We will be required to seek additional funding in the future and currently intend to do so through additional collaborations and/or licensing agreements, public or private equity offerings or debt financings, credit or loan facilities, or a combination of one or more of these funding sources. If we raise additional funds by issuing equity securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Any future debt financings we may do, if available to us, are likely to involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of our equity securities received any distribution of our corporate assets. If we raise additional funds through licensing or collaboration arrangements with third parties, we may have to relinquish valuable rights to our product candidates or grant licenses on terms that are not favorable to us. We also could be required to seek collaborators for product candidates at an earlier stage than otherwise would be desirable or relinquish some or all of our rights to certain product candidates or technologies that we otherwise would seek to develop or commercialize ourselves. Failure to obtain capital when needed on acceptable terms may force us to delay, limit or terminate our product development and commercialization of our current or future product candidates, which could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

We have incurred significant losses in every quarter since our inception and anticipate that we will continue to incur significant losses in the future.

We are a biotechnology company with a limited operating history of developing next generation immunotherapies for cancer, inflammation, and autoimmunity using *de novo* protein design technology. Investment in biotechnology is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval, or become commercially viable. We do not have any products approved by regulatory authorities for marketing or commercial sale, we have not generated any revenue from product sales to date, and all of our product candidates are in early clinical or preclinical development. We continue to incur significant expenses related to our ongoing operations. As a result, we are not profitable and have incurred losses in every reporting period since our inception as Aquinox in 2003. For the nine months ended September 30, 2022 and September 30, 2021, we reported net losses of $44.1 million and $45.5 million, respectively. For the years ended December 31, 2021 and 2020, we reported net losses of $60.7 million and $33.3 million, respectively. As of September 30, 2022, we had an accumulated deficit since our inception as Aquinox of $437.6 million.

We expect to continue to incur significant expenses and operating losses for the foreseeable future as we seek to identify, acquire, and conduct research and development of future product candidates, and potentially begin to commercialize any future products that may achieve regulatory approval. We may encounter unforeseen expenses, difficulties, complications, delays, and other unknown factors that may adversely affect our financial condition. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. Our prior losses and expected future losses have had, and will continue to have, an adverse effect on our financial condition. If we are unable to bring any of our product candidates or future product candidates through full clinical trials for any reason, or if such product candidates or future product candidates do not gain regulatory approval, or if approved, fail to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

The price of our common stock does not meet the requirements for continued listing on Nasdaq. If we fail to regain compliance with the minimum listing requirements, our common stock will be subject to delisting. Our ability to publicly or privately sell equity securities and the liquidity of our common stock could be adversely affected if our common stock is delisted.

The continued listing standards of the Nasdaq Stock Market, or Nasdaq, require, among other things, that the minimum bid price of a listed company's stock be at or above $1.00. If the closing minimum bid price is below $1.00 for a period of more than 30 consecutive trading days, the listed company will fail to be in compliance with Nasdaq's listing rules and, if it does not regain compliance within the grace period, will be subject to delisting. On October 26, 2022, we received a notice from the Nasdaq Listing Qualifications Department notifying us that for 30 consecutive trading days, the bid price of our common stock had closed below the minimum $1.00 per share requirement. In accordance with Nasdaq's listing rules, we were afforded a grace period of 180 calendar days, or until April 24, 2023, to regain compliance with the bid price requirement. In order to regain compliance, the bid price of our common stock must close at a price of at least $1.00 per share for a minimum of 10 consecutive trading days.

If we fail to regain compliance by April 24, 2023, we may be eligible for a second 180 day compliance period, provided that, on such date, we meet the continued listing requirement for market value of publicly held shares and all other applicable Nasdaq listing requirements (other than the minimum closing bid price requirement) and we provide written notice to Nasdaq of our intention to cure the deficiency during the second compliance period, by effecting a reverse stock split, if necessary. Such extension of the grace period would be subject to Nasdaq's discretion, and there can be no guarantee that we would be granted an extension.

We cannot provide any guarantee that we will regain compliance during the grace period or be able to maintain compliance with Nasdaq's listing requirements in the future. If we are not able to regain compliance during the grace period, or any extension of the grace period for which we may be eligible, our common stock will be subject to delisting. Delisting from Nasdaq could adversely affect our ability to raise additional financing through the public or private sale of equity securities, would significantly affect the ability of investors to trade our securities and

would negatively affect the value and liquidity of our common stock. Delisting could also have other negative results, including the potential loss of confidence by employees, the loss of institutional investor interest and fewer business development opportunities.

We have a limited operating history as a company developing therapies using* de novo *protein design technology, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Since we became Neoleukin Therapeutics, Inc., our operations have been primarily limited to organizing and staffing our company, acquiring product and technology rights, discovering and developing novel *de novo* proteins, and undertaking preclinical studies and early clinical development activities. We have not yet obtained regulatory approval for any product candidate. Consequently, evaluating our performance, viability or possibility of future success will be more difficult than if we had a longer operating history or approved products on the market.

We currently have no source of product revenue and may never become profitable.

To date, we have not generated any revenues from commercial product sales, or otherwise. Our ability to generate revenue from product sales and achieve profitability will depend upon our ability, alone or with any future collaborators, to successfully commercialize any products that we may develop, in-license, or acquire in the future. Even if we can successfully achieve regulatory approval for any product candidates or future product candidates, we do not know when any of these products will generate revenue from product sales for us, if at all. Our ability to generate revenue from any of our product candidates or future product candidates also depends on several additional factors, including our or any future collaborators' ability to:

- complete development activities, including the necessary clinical trials;
- complete and submit Biologics License Applications, or BLAs, to the U.S. Food and Drug Administration, or FDA, and obtain regulatory approval for indications for which there is a commercial market;
- complete and submit applications to, and obtain regulatory approval from, foreign regulatory authorities;
- set a commercially viable price for our products;
- establish and maintain supply and manufacturing relationships with third parties, and ensure adequate and legally compliant manufacturing of bulk drug substances and drug products to maintain that supply;
- develop a commercial organization capable of sales, marketing, and distribution for any products for which we obtain marketing approval and intend to sell ourselves in the markets in which we choose to commercialize on our own;
- find suitable distribution partners to help us market, sell, and distribute our approved products in other markets;
- obtain coverage and adequate reimbursement from third-party payors, including government and private payors;
- achieve market acceptance for our products, if any;
- establish, maintain, and protect our intellectual property rights; and
- attract, hire, and retain qualified personnel.

In addition, because of the numerous risks and uncertainties associated with biological product development, any future product candidates may not advance through development or achieve the endpoints of applicable clinical trials. Therefore, we are unable to predict the timing or amount of increased expenses, or when or if we will be able to achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we decide, or are required by the FDA or foreign regulatory authorities, to perform studies or trials in addition to those that we initially anticipate for any future product candidate. Even if we can complete the development and regulatory process for any product candidates or future product candidates, we anticipate incurring significant costs associated with commercializing these products.

Even if we can generate revenues from the sale of any product candidates or future product candidates that may be approved, we may not become profitable and may need to obtain additional funding to continue operations. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and may be forced to reduce our operations.

We will require additional capital to finance our operations which may not be available to us on acceptable terms, or at all. If we fail to obtain necessary financing, we may be unable to complete the development and potential commercialization of future product candidates.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. Our operations have consumed substantial amounts of cash since inception. If we identify and advance any current or future product candidates into clinical trials and launch and commercialize any product candidates for which we receive regulatory approval, we expect research and clinical development expenses, and our selling, general and administrative expenses to increase substantially. In connection with our ongoing activities, we believe that our existing cash, cash equivalents, and short-term investments will be sufficient to fund our operating requirements for at least the next 12 months. However, circumstances may cause us to consume capital more rapidly than we anticipate. We will likely require additional capital for the further development and potential commercialization of future product candidates and may also need to raise additional funds sooner to pursue a more accelerated development of future product candidates.

If we need to secure additional financing, fundraising efforts may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize future product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we do not raise additional capital when required or on acceptable terms, we may need to:

- seek strategic alliances for research and development programs at an earlier stage than we would otherwise desire or on terms less favorable than might otherwise be available;
- relinquish, or license on unfavorable terms, our rights to any future product candidates that we otherwise would seek to develop or commercialize ourselves; or
- significantly delay, scale back, or discontinue future clinical trials related to the development or commercialization of any of our future product candidates or cease operations altogether.

If we need to conduct additional fundraising activities and we do not raise additional capital in sufficient amounts or on terms acceptable to us, we may be prevented from pursuing development and commercialization efforts, which will have a material adverse effect on our business, operating results, and prospects.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this “Risk Factors” section. We have based this estimate on assumptions that may prove to be wrong, and we could spend our available capital resources sooner than we currently expect. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- our ability to identify additional product candidates for development;
- the initiation, progress, timing, costs, and results of clinical trials for any future product candidates;
- the estimated costs for discontinuing development of NL-201;
- the clinical development plans we establish for any future product candidates;
- if we in-license or acquire product candidates from third parties, the cost of in-licensing or acquisition;
- the achievement of milestones and our obligation to make milestone payments under our present or any future in-licensing agreements;
- the number and characteristics of product candidates that we discover, or in-license and develop;

- the outcome, timing, and cost of regulatory review by the FDA and comparable foreign regulatory authorities, including the potential for the FDA or comparable foreign regulatory authorities to require that we perform more studies than those that we currently expect;
- the cost to establish, maintain, expand, and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending, and enforcing any patent claims and maintaining and enforcing other intellectual property rights;
- the effects of the global macroeconomic trends, including supply chain disruptions, inflationary pressures, unemployment rates and impacts of a potential market recession, on our business and financial results;
- the effect of competing technological and market developments;
- the costs and timing of the implementation of commercial-scale outsourced manufacturing activities; and
- the costs and timing of establishing sales, marketing, distribution, and pharmacovigilance capabilities for any product candidates for which we may receive regulatory approval in territories where we choose to commercialize products on our own.

If we are unable to expand our operations or otherwise capitalize on our business opportunities due to a lack of capital, our business, results of operations, financial condition and cash flows, and future prospects could be materially adversely affected.

Risks Related to Discovery, Development, and Commercialization

Our product candidates are in early stages of development and may fail in development or suffer delays that materially and adversely affect their commercial viability. If we are unable to complete development of, or commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We are in the early stages of our development efforts. We have no products on the market, we have elected to discontinue development of NL-201, all of our remaining product candidates are still in [preclinical or] drug discovery stages, and we may not ever obtain regulatory approval for any of our product candidates. We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. Before obtaining regulatory approval for the commercial distribution of any future product candidates, we must conduct extensive preclinical tests and clinical trials to demonstrate the safety and efficacy in humans of our product candidates. Moreover, our development portfolio consists of targets and programs that are in earlier stages of discovery and preclinical development and may never advance to clinical-stage development. If we do not receive regulatory approvals for clinical testing and commercialization of our product candidates, we may not be able to continue our operations.

We may not have the financial resources to continue development of, or to enter into collaborations for, a product candidate if we experience any issues that cause or require us to delay or abandon preclinical or clinical trials or delay and/or prevent regulatory approval of or our ability to commercialize product candidates, including:

- preclinical study results showing the product candidate to be less effective than desired or to have harmful or problematic side effects;
- a failure to demonstrate that the dose for the product candidate has been optimized;
- negative or inconclusive results from our clinical trials or the clinical trials of others for product candidates similar to ours;
- product-related side effects experienced by patients in our clinical trials or by individuals using drugs or therapeutic biologics similar to our product candidates;
- our third-party manufacturers' inability to successfully manufacture our products or to meet regulatory specifications;
- inability of any third-party contract manufacturer to scale up manufacturing of our product candidates and those of our collaborators to supply the needs of clinical trials or commercial sales;

- delays in submitting Investigational New Drug, or INDs, or comparable foreign applications, or delays or failures in obtaining the necessary approvals from regulators to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA, the European Medicines Agency, or EMA, or other applicable regulatory authorities regarding the scope or design of our clinical trials;
- delays in enrolling patients in our clinical trials;
- high drop-out rates of our clinical trial patients;
- inadequate supply or quality of product candidate components or materials or other supplies necessary for the conduct of our clinical trials;
- inability to obtain alternative sources of supply for which we have a single source for product candidate components or materials;
- supply chain disruptions that may impact our ability to obtain materials for preclinical testing or supply materials to clinical testing sites or significantly increase our costs;
- greater than anticipated costs of our clinical trials;
- manufacturing costs, formulation issues, pricing or reimbursement issues or other factors that no longer make a product candidate economically feasible;
- harmful side effects or inability of our product candidates to meet efficacy endpoints during clinical trials;
- failure to demonstrate a benefit-risk profile acceptable to the FDA, EMA, or other applicable regulatory authorities;
- unfavorable inspection and review by the FDA, EMA, or other applicable regulatory authorities of one or more clinical trial sites or manufacturing facilities used in the testing and manufacture of any of our product candidates;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policy, and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or
- varying interpretations of our data by the FDA, EMA, or other applicable regulatory authorities.

Our inability to complete development of, or commercialize our product candidates, or significant delays in doing so due to one or more of these factors, could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

Further, cancer therapies are sometimes characterized as first-line, second-line, or third-line, and the FDA often approves new therapies initially only for advanced cancers, i.e. third-line or beyond. When cancer is detected early enough, first-line therapy, usually chemotherapy, surgery, radiation therapy, immunotherapy, hormone therapy, or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. Second- and third-line therapies are administered to patients when prior therapy is not effective. We expect that our product candidates will initially be targeted to second- or third-line patients, and that if those product candidates prove to be sufficiently beneficial in those initial trials, we would expect to seek subsequent approval in earlier lines of therapy. Any product candidates we develop, even if approved, may not be successfully approved for earlier lines of therapy, and, prior to any such approvals, we will likely have to conduct additional clinical trials, which are often very lengthy, expensive, and have a significant risk of failure.

Our business is heavily dependent on the success of our Neoleukin design process. Preclinical studies and clinical trials of our product candidates may not be successful, and if we are unable to commercialize these product candidates or experience significant delays in doing so, our business will be materially harmed.

Our business is heavily dependent on our ability to obtain regulatory approval of, and then successfully launch and commercialize, our product candidates. We have invested a significant portion of our efforts and financial resources in the development of advanced computational algorithms and other methods, including machine learning for the design of functional *de novo* proteins with an initial focus on key cytokine mimetics, which we refer to as Neoleukin *de novo* cytokine mimetics. We recently made a strategic decision to discontinue development for our lead product candidate, NL-201, and intend to focus our investment on early stage research of Neoleukin *de novo* proteins based, in part, on lessons learned from the clinical trial and preclinical studies of NL-201, which means we will continue for the near term to develop early stage product candidates. Our ability to generate commercial 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 our product candidates. Our product candidates may not be successful in clinical trials or receive regulatory approval. Even if they are successful in clinical trials, regulatory authorities may not complete their review in a timely manner, or additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials, and the review process. For example, the Oncology Center of Excellence within the FDA has recently advanced Project Optimus, which is an initiative to reform the dose optimization and dose selection paradigm in oncology drug development to emphasize selection of an optimal dose, which is a dose or doses that maximizes not only the efficacy of a drug but the safety and tolerability as well. This shift from the prior approach, which generally determined the maximum tolerated dose, may require sponsors to spend additional time and resources to further explore a product candidate's dose-response relationship to facilitate optimum dose selection in a target population. Other recent Oncology Center of Excellence initiatives have included Project FrontRunner, a new initiative with a goal of developing a framework for identifying candidate drugs for initial clinical development in the earlier advanced setting rather than for treatment of patients who have received numerous prior lines of therapies or have exhausted available treatment options. We are considering these policy changes as they relate to our programs.

Regulatory authorities may approve a product candidate for targets, disease indications, or patient populations that are not as broad as we intended or desired, approve more limited indications than requested, or require distribution restrictions or strong safety language, such as contraindications or boxed warnings. Regulatory authorities may also require Risk Evaluation and Mitigation Strategies, or REMS, or the performance of costly post-marketing clinical trials. Even if we successfully obtain regulatory approvals to market our product candidates, our revenues will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights. If the markets for patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of such products, if approved.

We plan to seek regulatory approval to commercialize our product candidates both in the United States and in selected foreign countries. In order to market and sell our 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 be required to expend significant resources to obtain regulatory approval, which may not be on a timely basis or successful at all, and to comply with ongoing regulations in these jurisdictions.

The success of our Neoleukin design process and our future product candidates will depend on many factors, including the following:

- successful completion of necessary preclinical studies to enable the initiation of clinical trials;
- successful enrollment of patients in, and the completion of, our clinical trials;

- obtaining adequate financing to perform the expensive clinical development programs anticipated for approval;
- receiving required regulatory authorizations for the development and approvals for the commercialization of our product candidates;
- establishing and maintaining arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity for our product candidates and their components;
- enforcing and defending our intellectual property rights and claims;
- achieving desirable therapeutic properties for our product candidates' intended indications;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with third parties;
- acceptance of our product candidates, if and when approved, by patients, the medical community, and third-party payors;
- achieving appropriate reimbursement, pricing, and payment coverage for our product candidates;
- effectively competing with other therapies, including those that are currently in development; and
- maintaining an acceptable safety profile of our product candidates through clinical trials and following regulatory approval.

If we do not achieve any one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

Clinical trials for our product candidates may reveal significant adverse events not seen in our preclinical studies and may result in a safety profile that could inhibit regulatory approval or market acceptance of those product candidates.

If significant adverse events or other side effects are observed in any of our future clinical trials, we may have difficulty recruiting patients to our clinical trials, patients may drop out of our trials, we may be required to revise, pause, delay, or abandon the trials or our development efforts of one or more product candidates altogether, we may be required to have more restrictive labeling, or we may experience the delay or denial of regulatory approval by applicable regulatory authorities. We, applicable regulatory authorities, or institutional review boards, or IRBs, may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects or patients in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance of the approved product due to its tolerability versus other therapies. Therapies involving cytokines have been known to cause side effects such as neurotoxicity and cytokine release syndrome, and there is no guarantee that these side effects can be avoided through *de novo* protein design.

Further, *de novo* proteins are a new class of therapeutics that have not been tested in humans prior to our initial Phase 1 clinical trial of NL-201. *De novo* proteins can be substantially different from all known proteins and as a result it is unknown to what extent, if any, *de novo* proteins may produce immunologic reactions in patients. Immunologic reactions could substantially limit the effectiveness of the treatment, the duration of treatment, or represent safety risks.

Additionally, if any of our product candidates receives marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits of the product outweigh its risks, which may include, among other things, a Medication Guide outlining the risks of the product for distribution to patients and a communication plan to health care practitioners. Furthermore, if we or others later identify undesirable side effects caused by any of our products, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label of such product;
- we may be required to change the way such a product is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these developments could materially harm our business, financial condition, and prospects.

If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.

From time to time, we estimate the timing of the anticipated accomplishment of various scientific, clinical, regulatory, and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are and will be based on numerous assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, or at all, the commercialization of our products may be delayed or never achieved and, as a result, our stock price may decline.

Our approach to the discovery and development of our therapeutic treatments is based on novel* de novo *protein design technology that are unproven and may not result in marketable products.

The success of our business depends primarily upon our ability to discover, develop, and commercialize a pipeline of product candidates using our Neoleukin *de novo* protein design process. Unlike traditional protein-based therapeutics that modify native proteins, our Neoleukin design process allows us to create new proteins from the ground up. Our design process uses advanced computational algorithms and methods to design functional *de novo* proteins that are hyper-stable, modifiable, and are designed to optimize desired intermolecular interactions and eliminate undesirable interactions. While we believe this approach will enable us to develop product candidates that may offer unique therapeutic benefits, the scientific basis of our efforts to develop product candidates using our Neoleukin design process is ongoing and may not result in viable product candidates.

While we had favorable preclinical study results related to NL-201, and monotherapy data that demonstrated engagement of the target receptor, expected pharmacodynamic changes for a potent IL-2/IL-15 agonist, and preliminary data that did not demonstrate significant immunogenicity even after multiple cycles of therapy, we determined that the resources required to continue clinical development would be better applied to advancing the next generation of de novo immunotherapies. We may not be successful in moving any of our future product candidates into clinical development, and any product candidates that we are able to bring into clinical trials may subsequently 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 one or more programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

Following our decision to discontinue development of NL-201 in November 2022, we will not have any product candidate currently being tested in a clinical trial. We have not tested any of our other product candidates in any clinical trials. We may ultimately discover that our Neoleukin design process and any product candidates resulting therefrom do not possess certain properties required for therapeutic effectiveness. Our product candidates may also be unable to remain stable in the human body for the period of time required for the drug to reach the target tissue, or they may trigger immune responses that inhibit the activity of the product candidate or that cause adverse side effects in humans. We may spend substantial funds attempting to mitigate these properties and may never succeed in doing so. In addition, product candidates based on our Neoleukin design process may demonstrate different chemical and pharmacological properties in patients than they do in laboratory studies. Our Neoleukin design process and any product candidates resulting therefrom may not demonstrate the same chemical and pharmacological properties in humans and may interact with human biological systems in unforeseen, ineffective, or harmful ways.

The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known, or extensively studied product candidates. Because the FDA has no prior experience with *de novo* proteins as therapeutics, we anticipate that this may increase the complexity, uncertainty, and length of the regulatory approval process for our product candidates. We or any future partners may be required to perform additional or unanticipated clinical trials to obtain approval or be subject to post-marketing testing requirements to maintain regulatory approval. If the products resulting from our Neoleukin design process and research programs prove to be ineffective, unsafe, or commercially unviable, our Neoleukin design process and pipeline would have little, if any, value, which would have a material and adverse effect on our business, financial condition, results of operations, and prospects.

Preclinical and clinical development involve a lengthy and expensive process, with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our current product candidates or any future product candidates.

Following the decision in November 2022 to discontinue development of NL-201, all of our product candidates will be in preclinical or earlier development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will receive regulatory approval. To obtain the requisite regulatory approvals to commercialize any product candidates, we must demonstrate through extensive preclinical studies and lengthy, complex, and expensive clinical trials that our product candidates are safe and effective in humans. Clinical testing can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process, or we may decide, as we did with NL-201, to stop development for strategic reasons at any time. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the success of later-stage clinical trials. The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful, and a clinical trial can fail at any stage of testing. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. Differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or to unfavorable safety profiles, notwithstanding promising results in earlier trials, and we could face similar setbacks. There is typically a high rate of failure of product candidates proceeding through clinical trials. Most product candidates that commence clinical trials are never approved as products, and there can be no assurance that any of our clinical trials will ultimately be successful or support clinical development of our product candidates.

Commencement of any future clinical trials for our product candidates is subject to finalizing the trial design and receiving approval from the FDA to proceed with clinical testing or similar approval from the EMA or other comparable foreign regulatory authorities. Even after we submit our IND or comparable submissions in other jurisdictions, the FDA, EMA, or comparable foreign regulatory authorities could disagree that we have satisfied their requirements to commence our clinical trials or disagree with our study design, which may require us to complete additional preclinical studies or amend our protocols or impose stricter conditions on the commencement of clinical trials.

We may encounter substantial delays in the commencement or completion of our clinical trials, or may be required to terminate or suspend such trials, which could result in increased costs to us or delay or limit our ability to generate revenue, adversely affecting our commercial prospects.

We may experience delays in initiating or completing clinical trials or may experience numerous unforeseen events during, or as a result of, any future clinical trials that we may conduct that could delay or prevent our ability to receive marketing approval or commercialize any future 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, ethics committees, FDA, EMA, or other applicable regulatory authorities, 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;
- clinical trial sites may deviate from trial protocol or drop out of a trial;
- clinical trials of any product candidates may fail to show safety or efficacy, or may produce negative or inconclusive results, which in turn may cause us to decide, or regulators to require us, to conduct additional preclinical studies or clinical trials, or we may decide to abandon product development programs;
- the number of subjects required for clinical trials of any product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or subjects may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs, or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants in our trials are being exposed to unacceptable health risks;
- the cost of clinical trials of any of our product candidates may be greater than we anticipate;
- 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 to initiate or complete a given clinical trial, or may be adversely impacted by global supply chain issues;
- we may be unable to obtain or manufacture sufficient quantities of our product candidates for use in clinical trials;
- reports from clinical testing of other therapies may raise safety or efficacy concerns about our product candidates; and
- we may fail to establish an appropriate safety profile for a product candidate based on clinical or preclinical data for such product candidate as well as data emerging from other molecules in the same class as our product candidate.

We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, or the FDA, EMA or other regulatory authorities, or if a clinical trial is recommended for suspension or termination by the Data Safety Monitoring Board, or the DSMB, for such trial. A suspension or termination may be imposed 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, EMA, or other 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 product or treatment, failure to establish or achieve clinically meaningful trial endpoints, changes in governmental regulations or administrative actions, lack of adequate funding to continue the clinical trial or other reasons related to our overall business strategy. For example, our IND for NL-201 was initially placed on clinical hold, and while the FDA removed that clinical hold, there is no guarantee that any future clinical trials we pursue may not experience a similar hold. In addition, we elected in November 2022 to discontinue development of NL-201 for strategic reasons, to allow us to focus our resources on the next generation of *de novo* protein design. Clinical studies may also be delayed or terminated as a result of ambiguous or negative interim results. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA, EMA, or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials.

Our product development costs will increase if we experience delays in clinical testing or obtaining marketing approvals. We do not know whether any of our clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates and may allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations. Any delays in our clinical development programs may harm our business, financial condition, and results of operations significantly.

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

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the number and location of clinical sites we enroll, the proximity of patients to clinical sites, the eligibility and exclusion criteria for the trial, the design of the clinical trial, the inability to obtain and maintain patient consents, the risk that enrolled participants will drop out before completion, competing clinical trials, and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs or therapeutic biologics that may be approved for the indications being investigated by us. Furthermore, we expect to rely on our collaborators, CROs, and clinical trial sites to ensure the proper and timely conduct of our future clinical trials, including the patient enrollment process, and we have limited influence over their performance. Additionally, we could encounter delays if treating physicians encounter unresolved ethical issues associated with enrolling patients in future clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles.

If we are unable to enroll a sufficient number of patients for our future clinical trials, it 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.

Preliminary, topline, and interim 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, and such changes in the final data may be material.

From time to time, we may publish preliminary or topline data from our recently terminated or future clinical trials, which is based on a preliminary analysis of then-available data. Those results and any related findings and conclusions are subject to change following a more comprehensive review of the more complete data related to the particular study or trial. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the preliminary or topline results that we report may differ from future results of the same studies or clinical trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Preliminary or topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary or topline data we previously published. Results from prespecified interim analyses that we may conduct 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. As a result, preliminary and topline data and prespecified interim analyses should be viewed with caution until the final data are available. Adverse differences between preliminary, topline, or interim data and final data could significantly harm our reputation and business prospects.

Failure to obtain regulatory approval would prevent any future product candidates from being marketed.

In order to market and sell our products, we must obtain marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval differs substantially from jurisdiction to jurisdiction. 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. Approval by a single regulatory authority does not ensure approval by other regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities. A failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market. If we are unable to obtain approval of any of our future product candidates by regulatory authorities, the commercial prospects of that product candidate may be significantly diminished and our business prospects could decline.

Recently enacted and future legislation, including potentially unfavorable pricing regulations or other healthcare reform initiatives, may increase the difficulty and cost for us to obtain marketing approval of, and commercialization of, our future product candidates and affect the prices we may obtain.

The regulations that govern, among other things, marketing approvals, coverage, pricing, and reimbursement for new drug products vary from country to country. In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our future product candidates, restrict or regulate post-approval activities, and affect our ability to successfully sell any product candidates for which we obtain marketing approval.
In the United States in recent years, Congress has considered reductions in Medicare reimbursement for drugs administered by physicians. The Centers for Medicare and Medicaid Services, or CMS, the agency that administers the Medicare program, also has the authority to revise reimbursement rates and to implement coverage restrictions for drugs. Cost reduction initiatives and changes in coverage implemented through legislation or regulation could decrease utilization of, and reimbursement for, any approved products, which in turn could affect the price we can receive for those products. For example, on September 9, 2021, the Biden administration published a wide-ranging list of policy proposals to lower prescription drug prices, including by allowing Medicare to negotiate prices and disincentivizing price increases, and to support market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase price transparency. These initiatives recently culminated in the enactment of the Inflation Reduction Act, or IRA, in August 2022, which will, among other things, allow the U.S. Department of Health and Human Services, or HHS, to negotiate the selling price of certain drugs and biologics that CMS reimburses under Medicare Part B and Part D, although only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for biologics) can be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. The negotiated prices, which will first become effective in 2026, will be capped at a statutory ceiling price beginning in October 2023, penalize drug manufacturers that increase prices of Medicare Part B and Part D drugs at a rate greater than the rate of inflation.

In addition, the law eliminates the “donut hole” under Medicare Part D beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and requiring manufacturers to subsidize, through a newly established manufacturer discount program, 10% of Part D enrollees’ prescription costs for brand drugs below the out-of-pocket maximum, and 20% once the out-of-pocket maximum has been reached. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges. While Medicare regulations apply only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in establishing their own coverage polices and reimbursement rates. Therefore, any reduction in reimbursement that results from federal legislation or regulation may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Affordable Care Act in an effort to, among other things, broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers and impose additional health policy reforms. The Affordable Care Act, among other things, also expanded manufacturers’ rebate liability under the Medicaid Drug Rebate Program, imposed a significant annual, nondeductible fee on companies that manufacture or import certain branded prescription drug products, and enacted substantial provisions affecting compliance, which may affect our business practices with healthcare practitioners. Certain provisions of the Affordable Care Act have been subject to judicial and Congressional challenges to repeal or replace certain aspects of the Affordable Care Act. On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued that the Affordable Care Act is unconstitutional in its entirety because the “individual mandate” was repealed by Congress. Thus, the Affordable Care Act will remain in effect in its current form. It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges in the future. It is uncertain how any such challenges and the healthcare measures of the Biden administration will impact the Affordable Care Act and in turn our business, prospects, financial condition, or results of operations.

Other legislative measures impacting federal expenditures on health care may also have an adverse impact on our business. For example, on August 2, 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation’s automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic, unless additional Congressional action is taken. The Medicare reductions phase back in starting with a 1% reduction in effect from April 1, 2022 to June 30, 2022 before increasing to the full 2% reduction. In addition, on January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and accordingly, our financial operations. Legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. Furthermore, in the past few years there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, including Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer’s patient programs, and reform government program reimbursement methodologies for drug products. We cannot be sure whether additional legislative changes will be enacted, or whether existing regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our future product candidates, if any, may be.

In the United States, the European Union and other potentially significant markets for our future product candidates, government authorities and third-party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which has resulted in lower

average selling prices. Furthermore, the increased emphasis on managed healthcare in the United States and on country and regional coverage, pricing, and reimbursement controls in the European Union will put additional pressure on product coverage, pricing, reimbursement, and utilization, which may adversely affect our business, results of operations, financial condition, cash flows, and future prospects. These pressures can arise from various sources, including but not limited to, rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies, and pricing in general.

Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenues we are able to generate from the sale of the product in that particular country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates even if our product candidates obtain marketing approval.

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

As we expand our operations outside of the United States, we must comply with numerous laws and regulations in each jurisdiction in which we plan to operate. We must also comply with U.S. laws applicable to the foreign operations of U.S. businesses and individuals, such as the Foreign Corrupt Practices Act, or FCPA. The creation and implementation of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The FCPA prohibits any U.S. individual or business from paying, offering, authorizing payment, or offering anything of value, directly or indirectly, to any foreign official, political party, or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the U.S. Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

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

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

The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The

SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

Even if we are able to commercialize our future product candidates, the products may not receive coverage and adequate reimbursement from third-party payors, which could harm our business.

Our ability to commercialize any products successfully will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government authorities, private health insurers, health maintenance organizations, and third-party payors. Patients who are prescribed medications for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Coverage and adequate reimbursement from government healthcare programs, such as Medicare and Medicaid, and private health insurers are critical to new product acceptance. Patients are unlikely to use our future product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. As a result, government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Third-party payors may also seek additional clinical evidence, beyond the data required to obtain marketing approval, demonstrating clinical benefits and value in specific patient populations before covering our products for those patients. We cannot be sure that coverage and adequate reimbursement will be available for any product that we commercialize and, if reimbursement is available, what that level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or are available only at limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, obtaining coverage does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sales, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based in part on existing reimbursement amounts for lower cost drugs or may be bundled into the payments for other services. Net prices for drugs 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 drugs from countries where they may be sold at lower prices than in the United States. Coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage and reimbursement determination process is often a time-consuming and costly process with no assurance that coverage and adequate reimbursement will be obtained or applied consistently. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

We have never marketed a drug before. If we are able to identify and develop or acquire a product candidate that is ultimately approved for sale but are unable to establish an effective sales force and marketing infrastructure or enter into acceptable third-party sales and marketing or licensing arrangements, we may be unable to generate any revenue.

We do not currently have an infrastructure for the sales, marketing, and distribution of pharmaceutical drug products, and the cost of establishing and maintaining such an infrastructure may exceed the cost-effectiveness of doing so. In addition, following the decision to discontinue development of NL-201 in November 2022, we do not have any product candidates in clinical development. If we are able to successfully advance any of our future product candidates through clinical development to approval by the FDA and comparable foreign regulatory authorities, we will need to either build our sales, marketing and distribution operations, including managerial and other non-technical capabilities, or make arrangements with third parties to perform these services. If we are unable to establish adequate sales, marketing, and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue and may not become profitable. We will be competing with many companies that have extensive and well-funded sales and marketing operations. Without an internal commercial organization or the support of a third party to perform sales and marketing functions, we may be unable to compete successfully against these more established companies.

Even if we are able to effectively hire a sales force and develop a marketing and sales infrastructure, our sales force and marketing team may not be successful in commercializing our product candidates, which would negatively affect our ability to generate revenue.

We may not be successful in our efforts to use our Neoleukin design process to expand our pipeline of product candidates and develop marketable products.

The success of our business depends in part upon our ability to discover, develop, and commercialize products based on our Neoleukin design process, which may fail to identify other potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval. If any of these events occur, we may be forced to abandon our development efforts for a program or for multiple programs, which would materially harm our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial, and human resources.

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

Because we have limited financial and managerial resources, we must choose the product candidates on which we focus our research and development efforts, which may require us to forgo or delay pursuit of opportunities with other product candidates that may ultimately have greater commercial potential. For instance, prior to November 2022, we were primarily focused on developing our lead product candidate, NL-201, and invested significant resources in the preclinical and Phase 1 clinical trial for that product candidate, but ultimately decided that our limited resources would be better spent on early stage research of the next generation *de novo* protein design and so elected to discontinue development of NL-201 even though that product candidate had demonstrated on target activity in reviews of preliminary data. Our resource allocation decisions may require us to make strategic decisions, which in turn may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing, or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We face substantial competition, including companies developing novel treatments and technology platforms in oncology. If these companies develop technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize product candidates may be adversely affected.

The development and commercialization of drugs is highly competitive. Our product candidates, if approved, will face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration. Most of our competitors have significantly greater resources than we do and we may not be able to successfully compete. We compete with a variety of multinational biopharmaceutical companies, specialized biotechnology companies, and emerging biotechnology companies, as well as with technologies and product candidates being developed at academic institutions, governmental agencies, and other public and private research institutions. Our competitors have developed, are developing, or will develop product candidates and processes competitive with our product candidates and processes. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments, including those based on novel technology platforms that enter the market. We believe that a significant number of products are currently under development and may become commercially available in the future for the treatment of conditions for which we are trying, or may try, to develop product candidates. There is intense and rapidly evolving competition in the biotechnology, biopharmaceutical, and interleukin and immunoregulatory therapeutics fields. Competition from many sources exists or may arise in the future. Our competitors include larger and better funded biopharmaceutical, biotechnological, and therapeutics companies, including companies focused on oncology therapeutics, as well as numerous small companies. Moreover, we also compete with current and future therapeutics developed at universities and other research institutions. Some of these companies are well-capitalized and, in contrast to us, have significant clinical experience, and may include our future partners. In addition, these companies compete with us in recruiting scientific and managerial talent.

Our success will depend partially on our ability to develop and commercialize therapeutics that are safer and more effective than competing products. Our commercial opportunity and success will be reduced or eliminated if competing products are safer, more effective, or less expensive than the therapeutics we develop.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales, and supply resources or experience than we have. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage, and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive, or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

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.

Our product candidates may face competition from other products that are the same as or similar to ours. If the FDA or comparable foreign regulatory authorities approve biosimilar versions of our product candidates, or such authorities do not grant our products appropriate periods of regulatory exclusivity, the sales of our products could be adversely impacted.

The Biologics Price Competition and Innovation Act of 2009, or the BPCIA, was enacted as part of the Affordable Care Act to establish an abbreviated pathway for the approval of biosimilar biological products (both highly similar and interchangeable biosimilar 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 first licensure date of the reference product licensed under a BLA. The law is complex and some provisions are still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

A biological product submitted for licensure under a BLA is eligible for a period of exclusivity that commences on the date of its licensure, unless its date of licensure is not considered a date of first licensure because it falls within an exclusion under the PBCIA. Our biological product candidates may qualify for the BPCIA's 12-year period of exclusivity, but there is a risk that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. There is also a risk that this exclusivity could be shortened due to congressional action or otherwise, potentially creating the opportunity for generic competition sooner than anticipated. For example, there have been efforts to decrease this period of exclusivity to a shorter timeframe—future proposed budgets, international trade agreements, and other arrangements or proposals may affect periods of exclusivity. Most states have enacted substitution laws that permit substitution of only interchangeable biosimilars. The extent to which a highly similar 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 decide to pursue accelerated approval for any of our product candidates, it may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval. If we are unable to obtain approval under an accelerated pathway, we may be required to conduct additional clinical trials beyond those that we contemplate, which could increase the expense of obtaining, reduce the likelihood of obtaining and/or delay the timing of obtaining, necessary marketing approvals.

In the future, we may decide to pursue accelerated approval for one or more of our product candidates. Under the FDA's accelerated approval program, the FDA may approve a drug or biological product for a serious or life-threatening disease or condition that provides a meaningful advantage over available therapies based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. For products granted accelerated approval, post-marketing confirmatory trials are required to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. These confirmatory trials must be completed with due diligence, and the FDA may require that the trial be designed, initiated, and/or fully enrolled prior to approval. If we were to pursue accelerated approval for a product candidate for a disease or condition, we would do so on the basis that there is no available therapy for that disease or condition. If standard of care were to evolve or if any of our competitors were to receive full approval on the basis of a confirmatory trial for a drug or biological product for a disease or condition for which we are seeking accelerated approval before we receive accelerated approval, the disease or condition would no longer qualify as one for which there is no available therapy, and accelerated approval of our product candidate would not occur. Many cancer therapies rely on accelerated approval, and the treatment landscape can change quickly as the FDA converts accelerated approvals to full approvals on the basis of successful confirmatory trials.

Moreover, the FDA may withdraw approval of any product candidate approved under the accelerated approval pathway if, for example:

- the trial or trials required to verify the predicted clinical benefit of our product candidate fail to verify such benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with such product;
- other evidence demonstrates that our product candidate is not shown to be safe or effective under the conditions of use;
- we fail to conduct any required post-approval trial of our product candidate with due diligence; or

- we disseminate false or misleading promotional materials relating to the relevant product candidate.

Recently, the accelerated approval pathway has come under scrutiny within the FDA and by Congress. The FDA has put increased focus on ensuring that confirmatory studies are conducted with diligence and, ultimately, that such studies confirm the benefit. For example, FDA has convened its Oncologic Drugs Advisory Committee to review what the FDA has called dangling or delinquent accelerated approvals where confirmatory studies have not been completed or where results did not confirm benefit. In addition, the Oncology Center of Excellence has recently announced Project Confirm, which is an initiative to promote the transparency of outcomes related to accelerated approvals for oncology indications and provide a framework to foster discussion, research and innovation in approval and post-marketing processes, with the goal to enhance the balance of access and verification of benefit for therapies available to patients with cancer and hematologic malignancies. Furthermore, in addition, Congress is considering various proposals to potentially make changes to the accelerated approval pathway, including proposals to increase the likelihood of withdrawal of approval in such circumstances.

Risks Related to Our Reliance on Third Parties

We rely on and expect to continue to rely on third parties to conduct certain of our preclinical studies and clinical trials. If those third parties do not perform as contractually required, fail to satisfy legal or regulatory requirements, miss expected deadlines or terminate the relationship, our development program could be delayed with potentially material and adverse effects on our business, financial condition, results of operations, and prospects.

We currently rely and intend to continue to rely in the future on third-party clinical investigators, CROs, clinical data management organizations, and consultants to assist or provide the design, conduct, supervision, and monitoring of preclinical studies and clinical trials of our product candidates, and will need to continue to rely on certain of those third parties who have assisted in our NL-201 Phase 1 clinical trial as we wind down development. Because we rely on, and intend to continue to rely on, these third parties and will not have the ability to conduct all preclinical studies or clinical trials independently, we will have less control over the timing, quality, and other aspects of preclinical studies and clinical trials than we would have had we conducted them on our own. Although we have agreements governing the activities of third parties, these investigators, CROs, and consultants will not be our employees, and we will have limited control over the amount of time and resources that they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources from our programs. The third parties with which we may contract might not be diligent, careful, or timely in conducting our preclinical studies or clinical trials, resulting in the preclinical studies or clinical trials being delayed or unsuccessful.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we will be responsible for ensuring that each of our preclinical studies and clinical trials are conducted in accordance with the general investigational plan and protocols for the trial as well as applicable legal and regulatory requirements. The FDA generally requires preclinical studies to be conducted in accordance with Good Laboratory Practices, or GLPs, and clinical trials to be conducted in accordance with Good Clinical Practices, or GCPs, including for designing, conducting, recording, and reporting the results of preclinical studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control will not relieve us of these responsibilities and requirements. If we or any of our third-party service providers fail to comply with applicable GCPs or other regulatory requirements, we or they may be subject to enforcement or other legal actions, the data generated in our trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional studies. Any adverse development or delay in our preclinical studies or clinical trials as a result of our reliance on third parties could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

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.

We rely on and expect to continue to rely on third-party manufacturers and suppliers to supply materials used in our research and development and preclinical testing as well as components of our product candidates. The loss of our third-party manufacturers or suppliers, or our or their failure to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, would materially and adversely affect our business.

We do not own or operate facilities for drug manufacturing, storage, distribution, or quality testing. We currently rely, and expect to continue to rely, on third-party contract manufacturers to manufacture bulk drug substances, drug products, raw materials, samples, components, or other materials and reports, and conduct fill-finish services. Reliance on third-party manufacturers may expose us to different risks than if we were to manufacture product candidates ourselves. Our third-party manufacturers may prioritize another customer's needs in front of ours, especially in the event of a global pandemic. Additionally, raw materials and components used in the manufacturing process, particularly those for which we have no other source or supplier, may not be available or may not be suitable or acceptable for use due to material or component defects, may be in short supply, and may significantly increase in price. There can be no assurance that our preclinical and clinical development product supplies will not be limited, or that they will be available at acceptable prices, if at all. In particular, any replacement of our manufacturer could require significant effort and expertise because there may be a limited number of qualified replacements. In addition, global supply chain disruption may hamper our ability to source materials needed for our research and development, including our preclinical trial programs, may increase our costs due to scarcity or may require us to buy materials on spec in advance of when we need it, which may impact our ability to budget or forecast expenditures, and may also hamper our ability to complete our preclinical trials on time, or at all.

The manufacturing process for a product candidate is subject to review by the FDA, EMA, or other applicable regulatory authorities. We, and our suppliers and manufacturers, must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as current Good Manufacturing Practices, or cGMPs. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA and foreign regulatory authorities. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA or other applicable regulatory authorities, we may not be able to rely on their manufacturing facilities for the manufacture of elements of our product candidates and approval may be delayed. Moreover, although we do not control the manufacturing process at our contract manufacturers and are completely dependent on them for compliance with current regulatory requirements, we are responsible for ensuring that our products comply with regulatory requirements. If any of our manufacturers fails to comply with such requirements or to perform its obligations 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 enter into an agreement with another third party, which we may not be able to do in a timely manner or on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such to another third party. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to enable us, or to have another third party, manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines, and we may be required to repeat some of the development program. The costs and delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We expect to continue to rely on third-party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. Any manufacturing facilities used to produce our products will be subject to periodic review and inspection by the FDA, EMA, or other applicable regulatory authorities, including for continued compliance with cGMP requirements, quality control, quality assurance, and corresponding maintenance of records and documents. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements, comply with cGMPs, or maintain a compliance status acceptable to the FDA, EMA, or other applicable regulatory authorities could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of future collaborators;
- subjecting third-party manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

Additionally, our contract manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. For example, the global outbreak of the COVID-19 pandemic resulted in extended shutdowns of businesses in the United States, Canada, and many other countries and had ripple effects to businesses around the world. Global health concerns, such as the COVID-19 pandemic, and the ensuing impacts on financial markets and supply chain logistics could also result in adverse effects to our manufacturing operations, including our ability to source raw materials and reagents. If our contract manufacturers were to encounter any of these difficulties, our ability to provide our product candidates to patients in preclinical and clinical trials, or to provide product for treatment of patients once approved, would be jeopardized.

Our third-party manufacturers may encounter difficulties in production. If we or any of our third-party manufacturers encounter such difficulties, our ability to provide supply of our product candidates for clinical trials, our ability to obtain marketing approval, or our ability to provide supply of our products for patients, if approved, could be delayed or stopped.

Our product candidates are biopharmaceuticals, and the process of manufacturing biopharmaceuticals is complex, time-consuming, highly regulated, and subject to multiple risks. Our contract manufacturers must comply with legal requirements, cGMPs, and guidelines for the bulk manufacturing, fill-finish services, packaging, and storage of biopharmaceuticals used in clinical trials and, if approved, marketed products. Our contract manufacturers may have limited experience in the manufacturing of cGMP batches.

Manufacturing biopharmaceuticals 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. If microbial, viral, or other contaminations are discovered at our third-party manufacturers' facilities, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business. Moreover, if the FDA determines that our third-party manufacturers' facilities are not in compliance with FDA laws and regulations, including those governing cGMPs, the FDA may deny approval of our application until the deficiencies are corrected or we replace the manufacturer in our application with a manufacturer that is in compliance.

In addition, there are risks associated with large scale manufacturing for clinical trials or commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, compliance with cGMPs, lot consistency and timely availability of raw materials. For example, certain resins used in the manufacture of biopharmaceuticals have recently experienced limited availability. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that manufacturers will be able to manufacture the approved product, or provide fill-finish services, to specifications acceptable to the FDA, EMA, or other applicable regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand. If our manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization, commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations, and prospects.

Scaling up a biopharmaceutical manufacturing process is a difficult and uncertain task, and our third-party manufacturers may not have the necessary capabilities to complete the implementation, manufacturing, and development process. If we are unable to adequately validate or scale-up the manufacturing process at our current manufacturers' facilities, we will need to transfer to another manufacturer and complete the manufacturing validation process, which can be lengthy. If we are able to adequately validate and scale-up the manufacturing process for our product candidates with a contract manufacturer, we will still need to negotiate with such contract manufacturer an agreement for commercial supply and it is not certain we will be able to come to agreement on terms acceptable to us.

We cannot assure you that any stability or other issues relating to the manufacture of any of our product candidates or products will not occur in the future. Our *de novo* protein product candidates may not demonstrate sufficient long-term stability to support a BLA submission or obtain approval, or the product shelf life may be limited by stability results. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. If our third-party manufacturers were to encounter any of these difficulties, our ability to provide any product candidates to patients in planned clinical trials and products to patients, once approved, would be jeopardized. Any delay, interruption or other issues that arise in the manufacture, fill- finish, packaging, or storage of clinical trial supplies could delay the completion of planned clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely. Any adverse development affecting clinical or commercial manufacturing of our product candidates or products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our product candidates or products. We may also have to take inventory write-offs and incur other charges and expenses for product candidates or products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. Accordingly, failures or difficulties faced at any level of our supply chain could adversely affect our business and delay or impede the development and commercialization of any of our product candidates or products, if approved, and could have an adverse effect on our business, prospects, financial condition, and results of operations.

As part of our process development efforts, we also may make changes to the manufacturing processes at various points during development, for various reasons, such as controlling costs, achieving scale, decreasing processing time, increasing manufacturing success rate or other reasons. Such changes carry the risk that they will not achieve their intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of our ongoing clinical trials or future clinical trials. In some circumstances, changes in the manufacturing process may require us to perform *ex vivo* comparability studies and to collect additional data from patients prior to undertaking more advanced clinical trials. For instance, changes in our process during the course of clinical development may require us to show the comparability of the product used in earlier clinical phases or at earlier portions of a trial to the product used in later clinical phases or later portions of the trial.

We may, in the future, seek to enter into collaborations with other third parties for the discovery, development, and commercialization of our product candidates. If our collaborators cease development efforts under our collaboration agreements, or if any of those agreements are terminated, these collaborations may fail to lead to commercial products, and we may never receive milestone payments or future royalties under these agreements.

We expect a significant portion of our future revenue and cash resources to be derived from collaboration agreements or other similar agreements into which we may enter in the future for research, development, and commercialization of other therapeutic technologies or product candidates. Biopharmaceutical companies are our likely future collaborators for any marketing, distribution, development, licensing, or broader collaboration arrangements. If we fail to enter into future collaborations on commercially reasonable terms, or at all, or such collaborations are not successful, we may not be able to execute our strategy to develop certain targets, product candidates, or disease areas that we believe could benefit from the resources of either larger biopharmaceutical companies or those specialized in a particular area of relevance.

Revenue from research and development collaborations depends upon continuation of the collaborations, payments for research and development services, and resulting options to acquire any licenses of successful product candidates, and the achievement of milestones, contingent payments, and royalties, if any, derived from future products developed from our research. If we are unable to successfully advance the development of our product candidates or achieve milestones, revenue and cash resources from milestone payments under our collaboration agreements will be substantially less than expected.

With respect to future collaboration agreements, we expect to have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Moreover, our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates may pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on preclinical studies or clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates 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;
- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;

- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

As a result of the foregoing, our current and any future collaboration agreements may not lead to development or commercialization of our product candidates in the most efficient manner or at all. 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. Any failure to successfully develop or commercialize our product candidates pursuant to our current or any future collaboration agreements could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

Moreover, to the extent that any of our future collaborators were to terminate a collaboration agreement, we may be forced to independently develop these product candidates, including funding preclinical studies or clinical trials, assuming marketing and distribution costs and defending intellectual property rights, or, in certain instances, abandon product candidates altogether, any of which could result in a change to our business plan and have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may have conflicts with our collaborators that could delay or prevent the development or commercialization of our product candidates.

We may have conflicts with our collaborators, such as conflicts concerning the interpretation of preclinical or clinical data, the achievement of milestones, the interpretation of contractual obligations, payments for services, development obligations, or the ownership of intellectual property developed during our collaboration. If any conflicts arise with any of our collaborators, such collaborator may act in a manner that is adverse to our best interests. Any such disagreement could result in one or more of the following, each of which could delay or prevent the development or commercialization of our product candidates, and in turn prevent us from generating revenues: unwillingness on the part of a collaborator to pay us milestone payments or royalties we believe are due to us under a collaboration, which could require us to raise additional capital; uncertainty regarding ownership of intellectual property rights arising from our collaborative activities, which could prevent us from entering into additional collaborations; unwillingness by the collaborator to cooperate in the development or manufacture of the product, including providing us with product data or materials; unwillingness on the part of a collaborator to keep us informed regarding the progress of its development and commercialization activities or to permit public disclosure of the results of those activities; initiating of litigation or alternative dispute resolution options by either party to resolve the dispute; or attempts by either party to terminate the agreement.

We may not successfully engage in strategic transactions, including any additional collaborations we seek, which could adversely affect our ability to develop and commercialize product candidates, impact our cash position, increase our expenses, and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as additional collaborations, acquisitions of companies, asset purchases, and out- or in-licensing of product candidates or technologies that we believe will complement or augment our existing business. In particular, we will evaluate and, if strategically attractive, seek to enter into additional collaborations, including with major biotechnology or biopharmaceutical companies. The competition for collaborators is intense, and the negotiation process is time-consuming and complex. Any new collaboration may be on terms that are not optimal for us, and we may not be able to maintain any new collaboration if, for example, development or approval of a product candidate is delayed, sales of an approved product candidate do not meet expectations or the collaborator terminates the collaboration. In addition, a significant number of recent business combinations among large pharmaceutical companies has resulted in a reduced number of potential future strategic partners. Our collaborators may consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the strategic partner's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed strategic partner's evaluation of a number of factors. These factors may include the design or results of clinical trials, the likelihood of approval by the FDA, EMA, or other applicable regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. Moreover, if we acquire assets with promising markets or technologies, we may not be able to realize the benefit of acquiring such assets if we are not able to successfully integrate them with our existing technologies. We may encounter numerous difficulties in developing, testing, manufacturing, and marketing any new products resulting from a strategic acquisition that delay or prevent us from realizing their expected benefits or enhancing our business.

We cannot assure you that following any such collaboration, or other strategic transaction, we will achieve the expected synergies to justify the transaction. For example, such transactions may require us to incur non-recurring or other charges, increase our near- and long-term expenditures and pose significant integration or implementation challenges or disrupt our management or business. These transactions would entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired products, product candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition, or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty, and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership, and the inability to retain key employees of any acquired business.

Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and would have a material and adverse effect on our business, financial condition, results of operations, and prospects. Conversely, any failure to enter any additional collaboration or other strategic transaction that would be beneficial to us could delay the development and potential commercialization of our product candidates and have a negative impact on the competitiveness of any product candidate that reaches market.

Risks Related to Our Business and Operations

The continued impact of the novel strain of coronavirus, SARS-CoV-2, which causes COVID-19 disease, could adversely impact our business.

Public health crises such as pandemics or similar outbreaks could adversely impact our business. The outbreak of a novel strain of coronavirus, which causes the disease called COVID-19, is a global pandemic. As a result of the COVID-19 pandemic, including the resurgence of cases relating to the spread of Delta and Omicron variants, or similar pandemics, we have experienced and may continue to experience disruptions that could severely impact our business, manufacturing, preclinical development activities, and preclinical studies, including:

- delays or disruptions in preclinical development activities, including non-clinical experiments and investigational new drug application-enabling GLP standard toxicology studies, due to unforeseen circumstances in supply chain;
- interruption or delays in the operations of the FDA and comparable foreign regulatory agencies, which may impact timelines for regulatory submission, trial initiation, and regulatory approval;
- interruption or delays in our CROs and collaborators meeting expected deadlines or complying with regulatory requirements related to preclinical development activities, preclinical studies, and clinical trial activities;
- interruptions of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, productions slowdowns, limited availability of raw materials, or stoppages and disruptions in delivery systems;
-
- diversion of healthcare resources away from the conduct of our preclinical development activities and preclinical studies;
-
- limitations on employee or collaborator resources that would otherwise be focused on the conduct of our preclinical development activities, preclinical studies, and clinical trial activities, including because of sickness of employees or their families, the desire of employees to avoid contact with large groups of people, an increased reliance on working from home, or mass transit disruptions; and
- reduced ability to engage with the medical and investor communities due to the cancellation of conferences scheduled throughout the year.

These and other factors arising from the COVID-19 pandemic could worsen in countries afflicted with COVID-19, or could return to countries where the pandemic has been partially contained, each of which could further adversely impact our ability to conduct preclinical development activities, preclinical studies, clinical trial activities, and our business generally, and could have a material adverse impact on our operations and our financial condition and results.

In addition, the trading prices for our common stock and other biopharmaceutical companies, as well as the broader equity and debt markets, have been highly volatile in part due to the COVID-19 pandemic and the resulting impact on economic activity. As a result, we may face difficulties raising capital when needed, and any such sales may be on unfavorable terms to us. Further, to the extent we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of existing stockholders will be diluted.

The extent to which the COVID-19 pandemic may impact our business, manufacturing, preclinical development activities, preclinical studies, and clinical trial activities and will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of COVID-19, the duration of the pandemic, the potential for a second pandemic after it is contained, travel restrictions, and actions to address the pandemic or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions, and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

We may experience difficulties in preparing our operations for potential future growth, which could adversely affect our business.

As of September 30, 2022, we had approximately 77 full-time employees. As we shift our focus away from development of NL-201 and toward early stage development of the next generation of *de novo* protein design, we expect to restructure our employee base, including a reduction in force for departments focused on clinical and technical operations matters, as well as changes in other areas of our operations. As we return to early stage development, we expect to have more limited experience in product development, and if we are able to advance any product candidates through preclinical studies and into clinical trials, we will need to rebuild and potentially expand our development and regulatory capabilities, which will also likely require us to contract with other organizations to provide manufacturing and other capabilities for us. In the future, we also expect to have to manage additional relationships with collaborators or partners, suppliers, and other organizations. Our ability to prepare for future growth will require us to continue to improve our operational, financial, and management controls, reporting systems, and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. Our inability to successfully manage our growth and expand our operations could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

Any inability to attract and retain qualified key management and technical personnel would impair our ability to implement our business plan.
We have experienced high turnover in the past year, and expect we may continue to experience high turnover as we make changes to our workforce in connection with the discontinuation of further development of NL-201 and the planned focus on early stage development of the next generation of d*e novo* protein design. The reduction in workforce announced in November 2022 may make retention of our current personnel both more important and more challenging. We cannot guarantee that we will be able to retain key employees necessary to carry out our revised strategic plan, and if such employees were to leave, we may not be able to identify and hire the personnel we need to replace them. Our success largely depends on the continued service of key management, advisors, scientists and other specialized personnel. We currently do not maintain key person insurance on any of these individuals. The loss of one or more members of our management team or other key employees or advisors could delay our research and development programs and have a material and adverse effect on our business, financial condition, results of operations, and prospects. The relationships that our key managers have cultivated within our industry make us particularly dependent upon their continued employment with us. We are dependent on the continued service of key scientific and other skilled personnel because of the nature of our research and development process, *de novo* protein design and technologies required to create product candidates, and the specialized nature of the regulatory approval process. Because our management team and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty.

Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. We also face competition for personnel from other companies, universities, public and private research institutions, government entities, and other organizations. Our future success will depend in large part on our continued ability to attract and retain other highly qualified scientific, technical, and management personnel, as well as personnel with expertise in clinical testing, manufacturing, governmental regulation, and commercialization. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover and develop product candidates will be limited which could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

Our relationships with healthcare professionals, principal investigators, consultants, customers (actual and potential) and third-party payors are and will be subject, directly and indirectly, to applicable anti-kickback, fraud and abuse, privacy, transparency, and other healthcare laws and regulations, which could expose us to penalties, including without limitation, civil, criminal, and administrative sanctions, civil penalties, damages, fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid, and other federal healthcare programs, integrity obligations, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations.

As a biopharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid, or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our future arrangements with third-party payors and customers who are in a position to purchase, recommend, and/or prescribe our product candidates for which we obtain marketing approval. These broadly applicable fraud and abuse and other healthcare laws and regulations may constrain our future business or financial arrangements and relationships with healthcare professionals, principal investigators, consultants, customers, and third-party payors and other entities, including our marketing practices, educational programs, and pricing policies. Restrictions under applicable federal and state healthcare laws and regulations that may affect our ability to operate include, but are not limited to, the following:

- the federal Anti-Kickback Statute, which, among other things, prohibits persons from knowingly and willfully soliciting, offering, receiving, providing, or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either 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 a federal healthcare program such as Medicare and Medicaid;
- federal civil and criminal false claims laws, including the federal civil False Claims Act, and civil monetary penalty laws which impose criminal and civil penalties, including through civil whistleblower or qui tam actions, and, among other things, prohibit individuals or entities from knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment or approval that are false or fraudulent, or from knowingly making a false statement to improperly avoid, decrease, or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which, among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items, or services relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its 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 the appropriate authorization by entities subject to the law, such as health plans, healthcare clearinghouses, and healthcare providers;

- the federal Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to "payments or other transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors), physician assistants, certain types of advance practice nurses, and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians (as defined above) and their immediate family members and payments or other "transfers of value" to such physician owners and their immediate family members; and
- analogous local, state, and foreign laws and regulations, including: state anti-kickback and false claims laws which may apply to our business practices, including, but not limited to, research, distribution, sales and marketing arrangements, and claims involving healthcare items or services reimbursed by state governmental and non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government; local, state, and foreign laws that require drug manufacturers to track gifts and other remuneration and items of value provided to healthcare professionals and entities and file reports relating to pricing and marketing information and/or register their pharmaceutical sales representatives; and local, state, and foreign laws that govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our internal operations and any business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Recent healthcare reform legislation has also strengthened these laws. For example, the Affordable Care Act, among other things, amends the intent requirement of the federal Anti-Kickback Statute, such that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act codified case law that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. It is possible that governmental authorities will conclude that our business practices may 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 these laws or any other governmental laws and regulations that may apply to us, we may be subject to penalties, including without limitation, significant civil, criminal, and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, integrity obligations, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Moreover, we expect there will continue to be federal, state, local and foreign laws and regulations, proposed and implemented, that could impact our operations and business. The extent to which future legislation or regulations, if any, relating to healthcare fraud abuse laws or enforcement, may be enacted or what effect such legislation or regulation would have on our business remains uncertain.

We may form strategic alliances in the future, and we may not realize the benefits of such alliances.

We may form strategic alliances, create joint ventures or collaborations, or enter into licensing arrangements with third parties that we believe will complement or augment our existing business. These relationships or those like them may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our stockholders, or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for any future drug candidates and programs because our research and development pipeline may be insufficient, our drug candidates and programs may be deemed to be at too early a stage of development for collaborative effort and third parties may not view our drug candidates and programs as having the requisite potential to demonstrate safety and efficacy. If we license products or businesses, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. We cannot be certain that, following a strategic transaction or license, we will achieve the revenues or specific net income that justifies such transaction. Any delays in entering into new strategic partnership agreements related to our drug candidates could also delay the development and commercialization of our drug candidates and reduce their competitiveness even if they reach the market.

Our employees, independent contractors, principal investigators, CROs, consultants, vendors, and collaboration partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, principal investigators, CROs, consultants, vendors, and collaboration partners, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state data privacy and security, fraud and abuse and other healthcare laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Specifically, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Employee misconduct could also involve the improper use or misrepresentation of information obtained in the course of clinical trials or creating fraudulent data in our pre-clinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct for our directors, officers, and employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, results of operations, financial condition, and cash flows from future prospects, including the imposition of significant fines or other sanctions.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We will face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and will face an even greater risk if we commercialize any of our product candidates. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;

- significant time and costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any product candidates that we may develop.

We currently maintain product liability insurance coverage for our clinical trials, but the amount may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage for each new clinical trial we begin and if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. 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.

We may engage in future acquisitions that could disrupt our business, cause dilution to our stockholders, and harm our business, results of operations, financial condition, and cash flows and future prospects.

We may, in the future, make acquisitions of, or investments in, companies that we believe have products or capabilities that are a strategic or commercial fit with our future product candidates and business or otherwise offer opportunities for our company. In connection with these acquisitions or investments, we may:

- issue stock that would dilute our stockholders' percentage of ownership;
- incur debt and assume liabilities; and
- incur amortization expenses related to intangible assets or incur large and immediate write-offs.

We may not be able to complete acquisitions on favorable terms, if at all. If we do complete an acquisition, we cannot assure you that it will ultimately strengthen our competitive position or that it will be viewed positively by customers, financial markets, or investors. Furthermore, future acquisitions could pose numerous additional risks to our operations, including:

- problems integrating the purchased business, products, or technologies;
- increases to our expenses;
- the failure to discover undisclosed liabilities of the acquired asset or company;
- diversion of management's attention from their day-to-day responsibilities;
- harm to our operating results or financial condition;
- entrance into markets in which we have limited or no prior experience; and
- potential loss of key employees, particularly those of the acquired entity.

We may not be able to complete any acquisitions or effectively integrate the operations, products or personnel gained through any such acquisition.

Our ability to use our U.S. net operating losses to offset future taxable income will be subject to Section 382 limitations and may be limited by other factors.

As of December 31, 2021, we had U.S. net operating losses, or NOLs, of $108.2 million, for federal tax purposes, for which we have recorded a full valuation allowance, and R&D credit carryovers of $2.4 million, which may be offset by future taxable income. The R&D credit carryforwards and certain of our NOL carryforwards will expire in various years beginning in 2028 if not used. Unused losses incurred in taxable years beginning on or prior to December 31, 2017 will carry forward to offset future taxable income, if any, until such unused losses expire. Under the Tax Cuts and Jobs Act, as modified by the CARES Act, unused U.S. federal NOLs generated in tax years beginning after December 31, 2017, will not expire and may be carried forward indefinitely, but the deductibility of such federal NOLs (particularly those generated in taxable years beginning after December 31, 2020) is limited to 80% of current year taxable income. It is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act or the CARES Act. Furthermore, use of certain of our NOLs and R&D credit carryforwards will be subject to annual limitations on their use as a result of ownership changes under the rules of Sections 382 and 383 of the Internal Revenue Code, or the Code that have historically occurred. Based on our Section 382 analysis to date, we underwent ownership changes in August 2015 and August 2019. As a result of these ownership changes, we believe that certain of our NOLs will be likely to expire before they are able to be used under Section 382. In addition, we may experience ownership changes in the future as a result of future changes in our stock ownership, some of which changes are outside of our control, and as a result, our ability to utilize NOL and R&D credit carryforwards could become further limited under Sections 382 and 383, and the tax benefits related to our NOLs and R&D credits may be diminished or lost. Any such disallowances may result in greater tax liabilities than we would incur in the absence of such a limitation and any increased liabilities could adversely affect our business, results of operations, financial condition, cash flow and future prospects. As a result, even if we attain profitability, we may be unable to use all or a material portion of our NOLs and other tax attributes, which could adversely affect our future cash flows.

Risks Related to Intellectual Property

If we are not able to obtain, maintain, and enforce patent protection and other intellectual property rights for our product candidates, our Neoleukin design process technology, or other proprietary technologies we may develop, the development and commercialization of our product candidates may be adversely affected.

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, for our product candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. Under our License Agreement with the University of Washington, dated July 8, 2019, as amended on October 29, 2020, effective July 24, 2020, and again on December 27, 2021, effective December 15, 2021, we have an exclusive license to develop and commercialize products covered by patent applications with claims covering the composition of matter of key molecule families as well as methods of using the computational algorithms that form the basis of the Neoleukin design process. However, we may not be able to apply for patents on certain aspects of our product candidates in a timely fashion or at all. Further, we may not be able to prosecute all necessary or desirable patent applications, or maintain, enforce, and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing, and prosecution of all patent applications that we license from third parties, or to maintain the rights to patents licensed to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Patents we currently hold, or in the future may 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 future issued or granted patents will not later be found to be invalid or unenforceable or that any future issued or granted patents will include claims that are sufficiently broad to cover our product candidates 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.

Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. 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 were the first to make the inventions claimed in our pending patent applications, or that we were the first to file for patent protection of such inventions.

The U.S. Patent and Trademark Office, or USPTO, and various foreign governmental patent agencies require compliance with a large number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. The standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and biopharmaceutical patents. As such, we do not know the degree of future protection that we will have on our proprietary products and technology. The process of obtaining patents is time consuming, expensive and sometimes unpredictable.

Once granted, for a given period after allowance or grant patents may remain open to opposition, interference, re-examination, post-grant review, *inter partes* review, nullification, or derivation action in court or before patent offices or similar proceedings, during which time third parties can raise objections against such initial grant. Such proceedings may continue for a protracted period of time and an adverse determination in any such proceedings could reduce the scope of the allowed or granted claims thus attacked, or could result in our patents being invalidated in whole or in part, or being held unenforceable, which could allow third parties to commercialize our product candidates and compete directly with us without payment to us. In addition, there can be no assurance that:

- others will not or may not be able to make, use or sell compounds that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or license;
- we or our licensors, or our future collaborators are the first to make the inventions covered by each of our issued patents and pending patent applications that we own or license;
- we or our licensors, or our future collaborators are the first to file patent applications covering certain aspects of our inventions;
- others will not independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- a third party may not challenge our patents and, if challenged, a court would hold that our patents are valid, enforceable and infringed;
- any issued patents that we own or have licensed or that we may license in the future will provide us with any competitive advantages, or will not be challenged by third parties;
- we may develop additional proprietary technologies that are patentable;
- the patents of others will not have a material or adverse effect on our business, financial condition, results of operations, and prospects; and
- our competitors do not conduct research and development activities in countries where we do not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.

If we or our licensors or collaborators fail to maintain patent applications and later-issued patents covering our product candidates, our competitors might be able to enter the market, which could have a material and adverse effect on our business, financial condition, results of operations, and prospects. In addition, if the breadth or strength of protection provided by our patent applications and later-issued patents is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

We could be required to incur significant expenses to strengthen our intellectual property rights, and our intellectual property rights may be inadequate to protect our competitive position.

The patent prosecution process is expensive and time-consuming, and we or our future potential licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our future potential licensors will fail to identify patentable aspects of inventions made in the course of our development and commercialization activities before it is too late to obtain patent protection on them. Further, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the expiration of the patent. However, the applicable authorities, including the FDA in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States, and these foreign laws may also be subject to change. For example, methods of treatment and manufacturing processes may not be patentable in certain jurisdictions. 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 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.

Our patent applications and the enforcement or defense of our issued patents may be impacted by the application of or changes in U.S. and foreign standards.

The standards that the USPTO and foreign patent offices use to grant patents are not always applied predictably or uniformly and can change. Consequently, our pending patent applications may not be allowed and, if allowed, may not contain the type and extent of patent claims that will be adequate to conduct our business as planned. Additionally, any issued patents we currently own or obtain in the future may have a shorter patent term than expected or may not contain claims that will permit us to stop competitors from using our technology or similar technology or from copying our product candidates. Similarly, the standards that courts use to interpret patents are not always applied predictably or uniformly and may evolve, particularly as new technologies develop. In addition, changes to patent laws in the United States or other countries may be applied retroactively to affect the validation enforceability, or term of our patent. For example, the U.S. Supreme Court has recently modified some legal standards applied by the USPTO in examination of U.S. patent applications, which may decrease the likelihood that we will be able to obtain patents and may increase the likelihood of challenges to patents we obtain or license. In addition, changes to the U.S. patent system have come into force under the Leahy-Smith America Invents Act, or the Leahy-Smith Act, which was signed into law in September 2011. The Leahy-Smith Act included a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a “first to file” system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in opposition, derivation, reexamination, inter-partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, which could adversely affect our competitive position.

While we cannot predict with certainty the impact the Leahy-Smith Act or any potential future changes to the U.S. or foreign patent systems will have on the operation of our business, the Leahy-Smith Act and such future changes could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, results of operations, financial condition and cash flows and future prospects.

Obtaining and maintaining any patent protection we may receive will depend on compliance with various procedural, document submissions, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. 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 noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our future licensors fail to maintain the patents and patent applications covering our product candidates, our competitive position would be adversely affected.

We may be subject to claims by third parties claiming ownership of what we regard as our own intellectual property, which may prevent, delay or otherwise interfere with our product discovery and development efforts.

Many of our employees, including our senior management, were previously employed at universities or at other biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Some of these employees, including members of our senior management, executed proprietary rights, non-disclosure and non-competition agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we, or these employees, have used or disclosed confidential information or intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. We are not aware of any threatened or pending claims related to these matters or concerning the agreements with our senior management, but in the future litigation may be necessary to defend against such claims. In addition, third parties may from time to time make claims over what we regard as our intellectual property, or we may get into disputes with licensors or licensees of our intellectual property rights over the interpretation of the license terms. If a third party claims that we infringe, misappropriate or otherwise violate their intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims that, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;
- substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages plus the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third-party licenses its product rights or proprietary technology to us, which it is not required to do, on commercially reasonable terms or at all;
- if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our product candidates;

- the requirement that we redesign our product candidates or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time; and
- 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.

Our licensors may have the right to terminate their license agreements with us or pursue damages or other legal remedies. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful and could result in a finding that such patents are unenforceable or invalid.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question.

In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. These types of mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). These types of proceedings could result in revocation or amendment to our patents such that they no longer cover our product candidates. The outcome for any particular patent following legal assertions of invalidity and unenforceability is unpredictable. If a defendant were to prevail on a legal assertion of invalidity and/ or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Defense of these types of claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

Conversely, we may choose to challenge the patentability of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings), or we may choose to challenge a third party's patent in patent opposition proceedings in the Canadian Intellectual Property Office, or CIPO, the European Patent Office, or EPO, or another foreign patent office. Even if successful, the costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, CIPO, EPO or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates or proprietary technologies.

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. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, that perception could have a substantial adverse effect on the price of our common stock. Any of the foregoing could have a material adverse effect on our business financial condition, results of operations and prospects.

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 for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturing organizations, consultants, advisors and other third parties. We also generally enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, 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. 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 both within and outside the United States may be less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

Although we expect all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not currently clear how the FDA's disclosure policies may change in the future, if at all.

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

Filing, prosecuting and defending patents on our product candidates throughout the world would be prohibitively expensive. 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 and our licensors or future collaborators 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 products and may export otherwise infringing products to territories where we have patent protection, but where enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful.

The requirements for patentability may differ in certain countries, particularly developing countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In India, unlike the United States, there is no link between regulatory approval of a drug and its patent status. Furthermore, generic or biosimilar drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' or collaborators' patents, requiring us or our licensors or collaborators to engage in complex, lengthy and costly litigation or other proceedings. Generic or biosimilar drug manufacturers may develop, seek approval for, and launch biosimilar versions of our products. In addition to India, certain countries in Europe and developing countries, including China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors or collaborators may have limited remedies if patents are infringed or if we or our licensors or collaborators 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 and our licensors' or collaborators' efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

Intellectual property rights do not necessarily provide sufficient protection of our technology or address all potential threats to any competitive advantage we may have.

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. The following examples are illustrative:

- Others may be able to make compounds that are the same as or similar to our future product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- It is possible that our pending patent applications will not lead to issued patents.
- It is possible that there are prior public disclosures that could invalidate our owned or exclusively licensed patents, as the case may be, or parts of our owned or exclusively licensed patents.
- It is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our product candidates or technology similar to ours.
- It is possible that our owned or exclusively licensed patents or patent applications omit one or more individuals that should be listed as inventors or include one or more individuals that should not be listed as inventors, which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable or such omitted individuals may grant licenses to third parties.
- Issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.
- Our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as 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 have engaged in scientific collaborations in the past and will continue to do so in the future and our collaborators may develop adjacent or competing products that are outside the scope of our patents.
- We may not develop additional proprietary technologies that are patentable.
- The patents of others may have an adverse effect on our business.

We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through acquisitions and exclusive licenses.

The growth of our business may depend in part on our ability to acquire, license or use third-party proprietary rights.

For example, our product candidates may require specific formulations to work effectively and efficiently, we may develop product candidates containing pre-existing pharmaceutical compounds, or we may be required by the FDA or comparable foreign regulatory authorities to provide a companion diagnostic test or tests with our product candidates, any of which could require us to obtain rights to use intellectual property held by third parties. In addition, with respect to any patents we may co-own with third parties, we may require licenses to such co-owners interest to such patents. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties we identify as necessary or important in our business operations. In addition, we may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. Were that to happen, we may need to cease use of the compositions or methods covered by those third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on those intellectual property rights, which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be nonexclusive, which means our competitors may also receive access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

We sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Even if we hold such an option, we may be unable to negotiate a license from the institution within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies that may be more established or have greater resources than we do may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More 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. There can be no assurance that we will be able to successfully complete these types of negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to develop or market. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of certain programs and our business financial condition, results of operations and prospects could suffer.

Some intellectual property that we have in-licensed 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.

Inventions contained within some of our in-licensed patents and patent applications may have been made using U.S. government funding or other non-governmental funding. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act, and implementing regulations. We rely on our licensors to ensure compliance with applicable obligations arising from such funding, such as timely reporting, an obligation associated with in-licensed patents and patent applications. The failure of our licensors to meet their obligations may lead to a loss of rights or the unenforceability of relevant patents. For example, the government could have certain rights in such in-licensed patents, including a non-exclusive license authorizing the government to use the invention or to have others use the invention on its behalf for non-commercial purposes. In addition, our rights in such in-licensed government-funded inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any of the foregoing could harm our business, financial condition, results of operations and prospects significantly.

Risks Related to Ownership of Our Common Stock

Our stock price has been and will likely continue to be volatile and may decline regardless of our operating performance, resulting in substantial losses for investors.

The trading price of our common stock has been, and is likely to continue to be, volatile for the foreseeable future. The trading price of our common stock could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this report, these factors include:

- the success of competitive products or technologies;
- regulatory actions with respect to our products or our competitors' products;
- actual or anticipated changes in our growth rate relative to our competitors;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- results of clinical trials, including both safety and efficacy, of any of our current or future product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our future product candidates or clinical development programs;
- the results of our efforts to in-license or acquire additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors; and
- general economic, industry and market conditions, such as market volatility and economic uncertainty due to rising interest rates, inflation, the war in Ukraine, and the COVID-19 pandemic.

In addition, the stock market in general, and pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of these risks or any of a broad range of other risks, including those described in this "Risk Factors" section and elsewhere in this report, could have a dramatic and material adverse impact on the market price of our common stock.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation, or certificate of incorporation, and amended and restated bylaws, or bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, or remove our current management. These include provisions that:

- permit our board of directors to issue up to 5,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that all vacancies on our board of directors, including as a result of newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide advance notice in writing, and also specify requirements as to the form and content of a stockholder's notice;
- not provide for cumulative voting rights, thereby allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election; and
- provide that special meetings of our stockholders may be called only by the board of directors or by such person or persons requested by a majority of the board of directors to call such meetings.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, who are responsible for appointing the members of our management. Because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. Under Delaware law, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other things, the board of directors has approved the transaction. Any provision of our certificate of incorporation or 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.

The exclusive forum provisions in our certificate of incorporation and bylaws may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims.

Our certificate of incorporation, to the fullest extent permitted by law, provides that the Court of Chancery of the State of Delaware will be the exclusive forum for: any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, or the DGCL, our certificate of incorporation, or our bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. This exclusive forum provision does not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934, as amended, or the Exchange Act. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision and asserts claims under the Securities Act of 1933, as amended, or the Securities Act, inasmuch as Section 22 of the Securities Act, creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rule and regulations thereunder. There is uncertainty as to whether a court would enforce such provision with respect to claims under the Securities Act, and our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

In April 2020, we amended and restated our bylaws to provide that the federal district courts of the United States of America will, to the fullest extent permitted by law, be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or a Federal Forum Provision. Our decision to adopt a Federal Forum Provision followed a decision by the Supreme Court of the State of Delaware holding that such provisions are facially valid under Delaware law. While there can be no assurance that federal or state courts will follow the holding of the Delaware Supreme Court or determine that the Federal Forum Provision should be enforced in a particular case, application of the Federal Forum Provision means that suits brought by our stockholders to enforce any duty or liability created by the Securities Act must be brought in federal court and cannot be brought in state court.

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 any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find the choice of forum provisions contained in our certificate of incorporation or bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, results of operations and financial condition.

We are no longer an "emerging growth company," however, we are still a "smaller reporting company," and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

Although we ceased to be an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act, on December 31, 2019, we are a "smaller reporting company," meaning that the market value of our stock held by non-affiliates is less than $700.0 million and our annual revenue is less than $100.0 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million. As a smaller reporting company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. 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 stock price may be more volatile.

We may become a "large accelerated filer" and have to comply with more rigorous disclosure and reporting requirements and regulations.

If we cease to be a "smaller reporting company" or a "non-accelerated filer" in the future, we may be subject to certain disclosure requirements that are applicable to other public companies that had not been applicable to us previously. These requirements include:

- compliance with the auditor attestation requirements in the assessment of our internal control over financial reporting once we are an accelerated filer or large accelerated filer;
- compliance with any requirement that may be adopted by the PCAOB regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements; and
- full disclosure and analysis obligations regarding executive compensation.

There can be no assurance that we will be able to comply with the applicable regulations in a timely manner, if at all. Inability to comply with these regulations could impact our ability to raise additional capital.

General Risk Factors

We may be subject to securities litigation, which is expensive and could divert management attention.

The trading price of our common stock has been and will continue to be volatile. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

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

Our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates together beneficially own a majority of our outstanding voting stock. These stockholders are able to determine the outcome of all matters requiring stockholder approval. For example, these stockholders are able to control elections of directors, amendments of our organizational documents, or approval 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 you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

If we fail to maintain an effective system of internal control over financial reporting in the future, we may not be able to accurately report our business, results of operations, financial condition and cash flows and future prospects, which may adversely affect investor confidence in us and, as a result, the value of our common stock.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures and that we furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. This assessment needs to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting that results in more than a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected on a timely basis. Section 404 of the Sarbanes-Oxley Act also generally requires an attestation from our independent registered public accounting firm on the effectiveness of our internal control over financial reporting. However, for as long as we are not an accelerated filer or large accelerated filer, we intend to take advantage of the exemption permitting us not to comply with the independent registered public accounting firm attestation requirement.

Our compliance with Section 404 will require that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge and compile the system and process documentation necessary to perform the evaluation needed to comply with Section 404. We may not be able to complete our evaluation, testing and any required remediation in a timely fashion. During the evaluation and testing process, if we fail to identify and to remediate any significant deficiencies or material weaknesses that may be identified, or encounter problems or delays in the implementation of internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the Nasdaq Stock Market, or Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

Our internal computer and information systems, or those used by our CROs, or other contractors or consultants, may fail or suffer security incidents (e.g., cyber-attacks) or other technical failures, which could result in a material disruption of our development programs and may result in extensive and costly legal compliance requirements.

Our *de novo* protein technology depends on sophisticated computational facilities and storage of vast amounts of data which could be lost or stolen. In the ordinary course of our business, we collect, store, and transmit confidential information, including intellectual property, proprietary business information and personal information. Despite the implementation of appropriate security measures, our internal computer and information systems and those of our current and any future CROs, and other contractors or consultants may become vulnerable to damage from security incidents (such as data breaches, viruses or other malicious code, coordinated attacks, data loss, phishing attacks, ransomware, denial of service attacks, or other security or information technology incidents caused by threat actors, technological vulnerabilities or human error), natural disasters, terrorism, war, including the recent conflict between Russia and Ukraine, and telecommunication and electrical failures.

While we have not experienced any such material system failure or security breach 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 data from completed or future preclinical studies and clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we 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, our competitive position could be harmed, and the further development and commercialization of our product candidates could be significantly delayed.

Our internal and outsourced information technology systems and infrastructure are also vulnerable to damage from natural disasters, terrorism, war, including Russia's recent invasion of Ukraine, telecommunication and electrical failures. System failures or outages, including any potential disruptions due to significantly increased global demand on certain cloud-based systems during the COVID-19 pandemic, could compromise our ability to perform our day-to-day operations, which could harm our ability to conduct business or delay our financial reporting. Such failures could materially adversely affect our operating results and financial condition.

Although we devote resources to protect our information systems, we realize that cyberattacks resulting in a security incident are a threat, and there can be no assurance of our efforts will prevent information security breaches that would result in business, legal, financial, or reputational harm to the Company, or would have a material adverse effect on our results of operations and financial condition. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. The COVID-19 pandemic is generally increasing the attack surface available to criminals, as more companies and individuals work online and work remotely, and as such, the risk of a cybersecurity incident potentially occurring, and our investment in risk mitigations against such an incident, is increasing.

Federal, state, and foreign government requirements include obligations of companies to notify regulators and/or individuals of security breaches involving personally identifiable information, which could result from breaches experienced by us or by our vendors, contractors, or organizations with which we have formed strategic relationships. Even though we may have contractual protections with such vendors, contractors, or other organizations, notifications and follow-up actions related to a security breach could impact our reputation and cause us to incur significant costs. Any failure to prevent or mitigate security breaches or improper access to, use, disclosure or other misappropriation of our data or consumers' personal data could result in significant legal liability, such as under state breach notification laws, federal law (including HIPAA/HITECH), and international law (e.g., GDPR). Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules and possible government oversight. Our failure to comply with such laws or to adequately secure the information we hold could result in significant liability or reputational harm and, in turn, a material adverse effect on our client base, member base and revenue. Further, if we are unable to generate or maintain access to essential patient samples or data for our research and development and manufacturing activities for our programs, our business could be materially adversely affected.

Business disruptions could seriously harm our future revenues 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 such as the COVID-19 pandemic and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We do not carry insurance for all categories of risk that our business may encounter. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of product candidates could be disrupted, if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. The ultimate impact on us, our significant suppliers and our general infrastructure of being consolidated in certain geographical areas is unknown, but our operations and financial condition could suffer in the event of a major earthquake, fire or other natural disaster. In addition, the long-term effects of climate change on general economic conditions and the pharmaceutical industry in particular are unclear, and may heighten or intensify existing risk of natural disasters. Further, any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our business, results of operations, financial condition and cash flows from future prospects.

Unfavorable global economic conditions or other geopolitical developments could adversely affect our business, financial condition, stock price, and results of operations.

In addition, our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the global financial crisis of 2007-2008 caused extreme volatility and disruptions in the capital and credit markets. Likewise, the capital and credit markets may be adversely affected by the recent conflict between Russia and Ukraine, and the possibility of a wider European or global conflict, and global sanctions imposed in response thereto. A severe or prolonged economic downturn, such as the global financial crisis, could result in a variety of risks to our business, including a decrease in the demand for our drug candidates and in our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy also could strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Further, the conflict in Ukraine could increase incidences of cybersecurity attacks against companies in the United States as retaliation for sanctions levied against Russia, which could increase our risk of being the subject of such an attack. We cannot anticipate all of the ways in which the foregoing, and the current economic climate, financial market conditions and geopolitical developments generally, could adversely impact our business. Furthermore, our stock price may decline due in part to the volatility of the stock market and any general economic downturn.

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

As a public company, we have incurred and will incur significant legal, accounting and other expenses that we did not incur as a private company, and these expenses will likely increase even more given we are no longer an "emerging growth company." We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Protection Act, as well as rules adopted, and to be adopted, by the SEC and Nasdaq. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have substantially increased our legal and financial compliance costs and made some activities more time-consuming and costly. The increased costs will increase our net loss. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

We have in the past and may in the future grant rights to some of our stockholders that require us to register the resale of our common stock or other securities on behalf of these stockholders and/or facilitate public offerings of our securities held by these stockholders, including in connection with potential future acquisition or capital-raising transactions. For example, in connection with our public offering of common stock on September 19, 2016, we entered into a registration rights agreement with the Baker Entities that together, based on information available to us, collectively beneficially owned approximately 45.1% of our common stock as of September 19, 2016. Under the registration rights agreement, we agree that, if at any time and from time to time after December 19, 2016, the Baker Entities demand that we register their shares of our common stock for resale under the Securities Act, we would be obligated to effect such registration. On January 6, 2017, pursuant to the registration rights agreement, we registered for resale, from time to time, up to 10,536,092 shares of our common stock held by the Baker Entities. Our registration obligations under this registration rights agreement cover all shares now held or hereafter acquired by the Baker Entities, would be in effect for up to ten years, and would include our obligation to facilitate certain underwritten public offerings of our common stock by the Baker Entities in the future. If the Baker Entities or any other holders of registration rights with respect to our common stock, by exercising their registration and/or underwriting rights or otherwise, sell a large number of our shares, or the market perceives that the Baker Entities or such holders intend to sell a large number of our shares, this could adversely affect the market price of our common stock. We have registered all currently reserved shares of common stock that we may issue under our equity compensation plans and intend to register in the future any additional reserved or issued shares of common stock. These registered shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. We have also filed a shelf registration statement covering the sale of up to $400.0 million of any combination of our common stock, preferred stock, debt securities, or warrants and may conduct one or more sales of securities pursuant to such registration statement, from time to time. In November 2021, we entered into an ATM "at-the-market" Equity Offering Sales Agreement, or Sales Agreement, with BofA Securities, Inc., or BofA, pursuant to which, from time to time, we may offer and sell through BofA up to $40.0 million of the common stock registered under the shelf registration statement pursuant to one or more "at the market" offerings. Sales of our common stock under the Sales Agreement with BofA could be subject to business, economic or competitive uncertainties and contingencies, many of which may be beyond our control, and which could cause actual results from the sale of our common stock to differ materially from expectations.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To raise capital, we may sell substantial amounts of common stock or securities convertible into or exchangeable for common stock. These future issuances of common stock or common stock-related securities, including the exercise of outstanding options and any additional shares issued in connection with acquisitions, if any, may result in material dilution to our stockholders. New investors could also gain rights, preferences, and privileges senior to those of holders of our common stock.

Pursuant to our 2014 Equity Incentive Plan, as amended, or 2014 Plan, our compensation committee is authorized to grant equity-based incentive awards to our directors, executive officers, and other employees and service providers, including officers, employees and service providers of our subsidiaries and affiliates. Future option grants and issuances of common stock under our 2014 Plan may have an adverse effect on the market price of our common stock.

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

The trading market for our common stock 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 securities or industry analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

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

None.

Item 3. Defaults Upon Senior Securities

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

Effective November 12, 2022, the Company's Board of Directors approved a strategic decision to discontinue further development of NL-201, and to move forward focusing the Company's investment in early stage pre-clinical development of the next generation of *de novo* proteins. The Board of Directors also approved a restructuring plan, including a reduction in force of approximately 40%. The Company's current best estimate of costs it will incur total between $6.3 million and $8.3 million, consisting of severance, benefits, costs associated with the discontinuation of further development of NL-201, and other costs. Approximately $1.1 million of these costs are expected to be non-cash expenses. The majority of these costs are expected to be incurred during the fourth calendar quarter of 2022 and the first half of 2023, and we expect the execution of the restructuring plan will be substantially complete by the second calendar quarter of 2023. The estimates of costs and expenses that we expect to incur in connection with the discontinued development of NL-201 and restructuring plan are subject to a number of assumptions and actual results may differ materially. We may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with the discontinued development of NL-201 and restructuring plan.

On November 12, 2022, the Company's Board of Directors approved a decision for Dr. Priti Patel to transition out of her role as our Chief Medical Officer. The Company is in the process of discussing the details of the transition, including her termination date. Dr. Patel is expected to receive post-employment benefits in accordance with her employment agreement.

Item 6. Exhibits

Number	Description
EX-31.1	Certification of Chief Executive Officer (Principal Executive and Financial Officer) pursuant to Rule 13a-14(a).
EX-32.1#	Certification of Chief Executive Officer (Principal Executive and Financial Officer) pursuant to 18 U.S.C. Section 1350.
101.INS	Inline XBRL Instance Document
101.SCH	Inline XBRL Taxonomy Extension Schema Document.
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document.
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)
#	This certification is deemed not filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (Exchange Act), or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act.

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.

Neoleukin Therapeutics, Inc.
(Registrant)

Date: November 14, 2022

/s/ Jonathan G. Drachman
Jonathan G. Drachman
President and Chief Executive Officer
(Principal Executive and Financial Officer)

Exhibit 31.1

CERTIFICATIONS

I, Jonathan G. Drachman, certify that:

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

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

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

4. The registrant's other certifying officer(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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

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

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

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

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

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

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

Date: November 14, 2022

/s/ Jonathan G. Drachman

Jonathan G. Drachman

President and Chief Executive Officer (Principal Executive and Financial Officer)

Exhibit 32.1

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

In connection with the Quarterly Report of Neoleukin Therapeutics, Inc. (the "Company") on Form 10-Q for the quarter ended September 30, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Jonathan G. Drachman, President and Chief Executive Officer of the Company certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of his knowledge:

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

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

IN WITNESS WHEREOF, the undersigned has set their hand hereto as of November 14, 2022.

/s/ Jonathan G. Drachman
Jonathan G. Drachman
President and Chief Executive Officer
(Principal Executive and Financial Officer)

This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Neoleukin Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.