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 August 31, 2022

OR

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

For the transition period from to

Commission File Number: 001-39398

NURIX THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware **(State or other jurisdiction of incorporation or organization)**	**27-0838048** **(I.R.S. Employer Identification No.)**
1700 Owens Street, Suite 205 **San Francisco, CA** **(Address of principal executive offices)**	**94158** **(Zip Code)**

Registrant's telephone number, including area code: (415) 660-5320

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	NRIX	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 (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). Yes ☒ No ☐

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

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

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

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

As of September 30, 2022, the Registrant had 47,147,781 shares of common stock, $0.001 par value per share, outstanding.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this Quarterly Report on Form 10-Q other than statements of historical fact, including statements concerning our business strategy and plans, future operating results and financial position, as well as our objectives and expectations for our future operations, are forward-looking statements.

In some cases, you can identify forward-looking statements by such terminology as "believe," "may," "will," "potentially," "estimate," "continue," "anticipate," "intend," "could," "would," "project," "plan," "expect" and similar expressions that convey uncertainty of future events or outcomes, although not all forward-looking statements contain these words. Forward-looking statements include, but are not limited to, statements about:

- the timing of investigational new drug application (IND) submissions for our drug candidates;
- the timing and conduct of our clinical trial programs for our lead drug candidates NX-2127, NX-1607, NX-5948, DeTIL-0255 and other drug candidates, including statements regarding the timing of initiation of clinical trials;
- the timing of, and our ability to obtain, marketing approvals for our lead drug candidates NX-2127, NX-1607, NX-5948, DeTIL-0255 and other drug candidates;
- our plans to pursue research and development of other drug candidates;
- the potential advantages of our DELigase platform and our drug candidates;
- the extent to which our scientific approach and DELigase platform may potentially address a broad range of diseases;
- the potential benefits of our arrangements with Sanofi S.A. and Gilead Sciences, Inc.;
- the timing of and our ability to obtain and maintain regulatory approvals for our drug candidates;
- the potential receipt of revenue from future sales of our drug candidates;
- the rate and degree of market acceptance and clinical utility of our drug candidates;
- our estimates regarding the potential market opportunity for our drug candidates;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for the manufacturing of our drug candidates;
- the impact of the ongoing coronavirus (COVID-19) pandemic, including the resurgence of cases relating to the spread of new variants, on our business, clinical trials, financial condition, liquidity and results of operations;
- the potential achievement of milestones and receipt of royalty payments under our collaborations;
- our ability to enter into additional collaborations with third parties;
- our intellectual property position;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the impact of government laws and regulations; and
- our competitive position.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our business, financial condition, results of operations, prospects, and financial needs. These forward-looking statements speak only as of the date of this Quarterly Report on Form 10-Q and are subject to a number of risks, uncertainties and assumptions described in the section titled "Risk Factors" and elsewhere in this Quarterly Report on Form 10-Q. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. We disclaim any intention or obligation to publicly update or revise any forward-looking statements for any reason or to conform such statements to actual results or revised expectations, except as required by law.

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PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

NURIX THERAPEUTICS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share amounts)
(unaudited)

	August 31, 2022	November 30, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 47,556	$ 80,506
Marketable securities, current	296,922	215,214
Accounts receivable	—	6,000
Income tax receivable	—	204
Prepaid expenses and other current assets	10,393	9,194
Total current assets	354,871	311,118
Marketable securities, non-current	69,125	137,189
Operating lease right-of-use assets	13,848	14,005
Property and equipment, net	16,501	11,340
Restricted cash	901	286
Other assets	4,092	2,833
Total assets	$ 459,338	$ 476,771
Liabilities and stockholders′ equity		
Current liabilities:		
Accounts payable	$ 6,053	$ 6,650
Accrued expenses and other current liabilities	19,609	14,549
Operating lease liabilities, current	5,496	3,847
Deferred revenue, current	36,342	41,212
Total current liabilities	67,500	66,258
Operating lease liabilities, net of current portion	7,745	9,189
Deferred revenue, net of current portion	41,548	59,022
Total liabilities	116,793	134,469
Commitments and contingencies (Note 6)		
Stockholders′ equity:		
Preferred stock, $0.001 par value— 10,000,000 shares authorized as of August 31, 2022 and November 30, 2021; no shares issued and outstanding as of August 31, 2022 and November 30, 2021	—	—
Common stock, $0.001 par value— 500,000,000 shares authorized as of August 31, 2022 and November 30, 2021; 47,147,781 and 44,664,371 shares issued and outstanding as of August 31, 2022 and November 30, 2021, respectively	47	45
Additional paid-in capital	700,775	563,757
Accumulated other comprehensive loss	(3,742)	(608)
Accumulated deficit	(354,535)	(220,892)
Total stockholders′ equity	342,545	342,302
Total liabilities and stockholders′ equity	$ 459,338	$ 476,771

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

NURIX THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share amounts)
(unaudited)

	Three Months Ended August 31,		Nine Months Ended August 31,	
	2022	2021	2022	2021
Collaboration revenue	$ 10,791	$ 10,252	$ 31,844	$ 22,354
Operating expenses:				
Research and development	47,761	30,906	138,391	79,903
General and administrative	9,748	8,343	28,630	22,384
Total operating expenses	57,509	39,249	167,021	102,287
Loss from operations	(46,718)	(28,997)	(135,177)	(79,933)
Interest and other income, net	1,009	39	1,534	528
Loss before income taxes	(45,709)	(28,958)	(133,643)	(79,405)
Provision for (benefit from) income taxes	—	(123)	—	87
Net loss	$ (45,709)	$ (28,835)	$ (133,643)	$ (79,492)
Net loss per share, basic and diluted	$ (0.90)	$ (0.65)	$ (2.85)	$ (1.88)
Weighted-average number of shares outstanding, basic and diluted	50,868,542	44,374,389	46,835,776	42,344,420

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

NURIX THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)
(unaudited)

	Three Months Ended August 31,		Nine Months Ended August 31,	
	2022	2021	2022	2021
Net loss	$ (45,709)	$ (28,835)	$ (133,643)	$ (79,492)
Other comprehensive loss, net of tax:				
Unrealized loss on available-for-sale securities	(657)	(89)	(3,134)	(146)
Total comprehensive loss	$ (46,366)	$ (28,924)	$ (136,777)	$ (79,638)

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

NURIX THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands, except share amounts)
(unaudited)

	Common stock		Additional paid-in capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity
	Shares	Amount				
Balance as of November 30, 2020	38,864,872	$ 39	$ 393,841	$ 87	$ (103,698)	$ 290,269
Exercise of stock options	190,825	—	394	—	—	394
Repurchase of unvested early exercised stock options	(971)	—	—	—	—	—
Vesting of early-exercised stock options	—	—	40	—	—	40
Issuance under employee stock purchase plan	64,589	—	1,043	—	—	1,043
Stock-based compensation	—	—	2,700	—	—	2,700
Unrealized loss on available-for-sale securities	—	—	—	(38)	—	(38)
Net loss	—	—	—	—	(24,275)	(24,275)
Balance as of February 28, 2021	39,119,315	39	398,018	49	(127,973)	270,133
Issuance of common stock in connection with equity offering, net of offering costs of $643	5,175,000	5	150,152	—	—	150,157
Exercise of stock options	109,232	—	241	—	—	241
Vesting of early-exercised stock options	—	—	104	—	—	104
Stock-based compensation	—	—	3,944	—	—	3,944
Unrealized loss on available-for-sale securities	—	—	—	(19)	—	(19)
Net loss	—	—	—	—	(26,382)	(26,382)
Balance as of May 31, 2021	44,403,547	44	552,459	30	(154,355)	398,178
Exercise of stock options	114,182	1	583	—	—	584
Vesting of early-exercised stock options	—	—	49	—	—	49
Issuance under employee stock purchase plan	38,875	—	1,017	—	—	1,017
Stock-based compensation	—	—	4,313	—	—	4,313
Unrealized loss on available-for-sale securities	—	—	—	(89)	—	(89)
Net loss	—	—	—	—	(28,835)	(28,835)
Balance as of August 31, 2021	44,556,604	$ 45	$ 558,421	$ (59)	$ (183,190)	$ 375,217

	Common stock		Additional paid-in capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity
	Shares	Amount				
Balance as of November 30, 2021	44,664,371	$ 45	$ 563,757	$ (608)	$ (220,892)	$ 342,302
Exercise of stock options	117,870	—	424	—	—	424
Vesting of early-exercised stock options	—	—	47	—	—	47
Issuance under employee stock purchase plan	71,207	—	1,064	—	—	1,064
Stock-based compensation	—	—	6,071	—	—	6,071
Unrealized loss on available-for-sale securities	—	—	—	(1,458)	—	(1,458)
Net loss	—	—	—	—	(42,533)	(42,533)
Balance as of February 28, 2022	44,853,448	45	571,363	(2,066)	(263,425)	305,917
Exercise of stock options	173,155	—	432	—	—	432
Vesting of restricted stock units	13,465	—	—	—	—	—
Vesting of early-exercised stock options	—	—	35	—	—	35
Stock-based compensation	—	—	6,775	—	—	6,775
Unrealized loss on available-for-sale securities	—	—	—	(1,019)	—	(1,019)
Net loss	—	—	—	—	(45,401)	(45,401)
Balance as of May 31, 2022	45,040,068	45	578,605	(3,085)	(308,826)	266,739
Issuance of pre-funded warrants, net of issuance costs of $234	—	—	94,759	—	—	94,759
Issuance of common stock in "at the market" financing, net of issuance costs of $672	2,000,000	2	19,326	—	—	19,328
Exercise of stock options	24,147	—	174	—	—	174
Vesting of restricted stock units	18,469	—	—	—	—	—
Vesting of early-exercised stock options	—	—	32	—	—	32
Issuance under employee stock purchase plan	65,097	—	891	—	—	891
Stock-based compensation	—	—	6,988	—	—	6,988
Unrealized loss on available-for-sale securities	—	—	—	(657)	—	(657)
Net loss	—	—	—	—	(45,709)	(45,709)
Balance as of August 31, 2022	47,147,781	$ 47	$ 700,775	$ (3,742)	$ (354,535)	$ 342,545

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

NURIX THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)
(unaudited)

	Nine Months Ended August 31,	
	2022	**2021**
Cash flows from operating activities		
Net loss	$ (133,643)	$ (79,492)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	3,730	2,033
Stock-based compensation	19,834	10,957
Net amortization (accretion) of premium (discount) on marketable securities	1,076	1,100
Loss on disposal of property and equipment	9	128
Amortization of operating lease right-of-use assets	4,041	2,439
Other	201	—
Changes in operating assets and liabilities:		
Accounts receivable	6,000	—
Income tax receivable	—	3,642
Prepaid expenses and other assets	(2,250)	(6,040)
Accounts payable	984	727
Deferred revenue	(22,344)	10,647
Operating lease liabilities	(3,679)	(2,432)
Accrued expenses and other liabilities	4,189	2,837
Net cash used in operating activities	(121,852)	(53,454)
Cash flows from investing activities		
Purchases of marketable securities	(212,455)	(257,813)
Sales of marketable securities	—	6,994
Maturities of marketable securities	194,324	183,890
Purchases of property and equipment	(9,679)	(4,799)
Net cash used in investing activities	(27,810)	(71,728)
Cash flows from financing activities		
Proceeds from issuances of pre-funded warrants, net of issuance costs	94,942	—
Proceeds from issuances of common stock in equity financing, net of issuance costs	19,400	150,157
Proceeds from exercise of stock options	1,030	1,166
Proceeds from issuance under employee stock purchase plan	1,955	2,060
Repurchase of unvested early exercised stock options	—	(1)
Net cash provided by financing activities	117,327	153,382
Net (decrease) increase in cash, cash equivalents and restricted cash	(32,335)	28,200
Cash, cash equivalents and restricted cash at beginning of period	80,792	119,526
Cash, cash equivalents and restricted cash at end of period	$ 48,457	$ 147,726
Supplemental disclosures of non-cash investing and financing activities:		
Additions to property and equipment included in accounts payable and accrued expenses and other liabilities	$ 1,726	$ 839
Vesting of early exercised stock options	$ 114	$ 193
Issuance costs related to pre-funded warrants included in accrued expenses and other liabilities	$ 183	$ —
Deferred issuance costs recognized related to equity financing	$ 72	$ —

	As of August 31,	
	2022	**2021**
Reconciliation of cash, cash equivalents and restricted cash:		
Cash and cash equivalents	$ 47,556	$ 147,440
Restricted cash	901	286
Total cash, cash equivalents and restricted cash	$ 48,457	$ 147,726

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

1. Organization

Description of Business

Nurix Therapeutics, Inc. (the Company) was incorporated in the state of Delaware on August 27, 2009 and is headquartered in San Francisco, California. The Company is a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of small molecule and cell therapies based on the modulation of cellular protein levels as a novel treatment approach for cancer and other challenging diseases. Leveraging the Company's expertise in E3 ligases together with its proprietary DNA-encoded libraries, the Company has built DELigase, an integrated discovery platform to identify and advance novel drug candidates targeting E3 ligases, a broad class of enzymes that can modulate proteins within the cell. Targeted Protein Modulation, our drug discovery approach, either harnesses or inhibits the natural function of E3 ligases within the ubiquitin-proteasome system to selectively decrease or increase cellular protein levels to treat disease.

Initial Public Offering

On July 23, 2020, the Company's registration statement on Form S-1 (File No. 333-239651) relating to its initial public offering (IPO) of common stock became effective. The IPO closed on July 28, 2020 at which time the Company issued 11,000,000 shares of its common stock at a price to the public of $19.00 per share. In addition, the underwriters exercised their option to purchase an additional 1,550,000 shares of the Company's common stock on July 31, 2020, and this transaction closed on August 4, 2020. Net proceeds from the IPO were $218.1 million, after deducting underwriting discounts and commissions of $16.7 million and expenses of $3.6 million.

Follow-on Offering

In March 2021, the Company completed a follow-on offering and issued 5,175,000 shares of common stock (including the exercise by the underwriters of their option to purchase an additional 675,000 shares of common stock) at a price to the public of $31.00 per share for net proceeds of $150.2 million, after deducting underwriting discounts and commissions of $9.6 million and expenses of $0.6 million.

Equity Distribution Agreement

In August 2021, the Company filed a shelf registration statement on Form S-3 with the Securities and Exchange Commission (SEC). This shelf registration statement, which includes a base prospectus, allows the Company at any time to offer and sell registered common stock, preferred stock, debt securities, warrants, subscriptions rights and or units or any combination of securities described in the prospectus in one or more offerings. In addition, in August 2021, the Company entered into an Equity Distribution Agreement with Piper Sandler & Co. (Piper Sandler) pursuant to which, from time to time, the Company may offer and sell through Piper Sandler up to $150.0 million of the common stock registered under the shelf registration statement pursuant to one or more "at the market" offerings.

The Company is not required to sell any shares at any time during the term of the Equity Distribution Agreement. The Company agreed to pay Piper Sandler a commission of 3% of the gross sales price of any shares sold pursuant to the Equity Distribution Agreement. In June 2022, the Company issued and sold 2,000,000 shares of common stock under the Equity Distribution Agreement at a price of $10.0001 per share of common stock for net proceeds of approximately $19.3 million, after deducting offering commissions and expenses paid by the Company. As of August 31, 2022, the Company had $130.0 million of common stock remaining available for sale under the Equity Distribution Agreement.

Registered Direct Offerings

In July 2022, the Company entered into separate securities purchase agreements with certain purchasers to issue and sell pre-funded warrants to purchase an aggregate of 6,814,920 shares of the Company's common stock in registered direct offerings (RDOs) at a price of $13.939 per pre-funded warrant. Net proceeds from the RDOs were approximately $94.8 million, after deducting offering expenses of $0.2 million. Refer to Note 7 for more information regarding the pre-funded warrants issued in the RDOs.

Liquidity and Management Plans

Since inception, the Company has generally incurred significant losses and negative net cash flows from operations. As of August 31, 2022, the Company had an accumulated deficit of $354.5 million and will require substantial additional capital for research and development activities. The Company anticipates incurring additional losses until such time, if ever, that it can generate significant sales of its drug candidates currently in development. As of August 31, 2022, the Company had cash, cash equivalents and marketable securities of $413.6 million.

Management believes that its cash, cash equivalents and marketable securities are sufficient to continue operating activities for at least 12 months following the issuance date of these condensed consolidated financial statements. Future capital requirements will depend on many factors, including the timing and extent of spending on research and development and payments the Company may receive under its collaboration agreements with Sanofi S.A. (Sanofi) and Gilead Sciences, Inc. (Gilead) or future collaboration agreements, if any. There can be no assurance that, in the event the Company requires additional financing, such financing will be available at terms acceptable to the Company if at all. If additional capital is not available, failure to generate sufficient cash flows from operations, raise additional capital and reduce discretionary spending could have a material adverse effect on the Company's ability to achieve its intended business objectives.

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company's condensed consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles (U.S. GAAP) and applicable rules and regulations of the SEC regarding interim financial reporting. The Company's condensed consolidated financial statements have been prepared on the same basis as the annual financial statements and reflect, in the opinion of management, all adjustments of a normal and recurring nature that are necessary for the fair statement of the Company's financial position as of and for the three and nine months ended August 31, 2022. The condensed consolidated balance sheet as of November 30, 2021 was derived from the audited annual financial statements as of that date. Certain information and footnote disclosures normally included in financial statements prepared in accordance with U.S. GAAP have been condensed or omitted from these interim financial statements. These interim financial statements and related disclosures have been prepared with the presumption that users of the interim financial statements have read or have access to the audited annual financial statements for the preceding fiscal year. Accordingly, these financial statements should be read in conjunction with the audited annual financial statements and notes thereto contained in the Company's Annual Report on Form 10-K for the year ended November 30, 2021, as filed with the SEC. These interim results are not necessarily indicative of results to be expected for the full fiscal year or any future interim period. Certain prior year amounts have been reclassified for consistency with the current year cash flow presentation. The reclassification did not impact total cashflow from operating, investing or financing activities.

Principles of Consolidation

The accompanying condensed consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries, including DeCART Therapeutics Inc, which was legally dissolved in July 2022. All intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities at the date of the financial statements and reported amounts of revenues and expenses during the reporting period. On an ongoing basis, management evaluates its estimates, including those related to the useful lives of long-lived assets, the measurement of stock-based compensation, accruals for research and development activities, income taxes and revenue recognition. The Company bases its estimates on historical experience and on other relevant assumptions that are reasonable under the circumstances. Actual results could materially differ from those estimates. Refer to Note 3 for more information regarding the estimates related to revenue recognition.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentration of credit risk consist of cash, cash equivalents and marketable securities. The Company's marketable securities consist of debt securities issued by highly rated corporate entities, the U.S. federal government or state and local governments. The Company's exposure to any individual corporate entity is limited by policy. Deposits may, at times, exceed federally insured limits. The Company invests its cash equivalents in highly rated money market funds. During the periods presented, the Company has not experienced any losses on its deposits of cash, cash equivalents or marketable securities.

Other Risks and Uncertainties

The Company is subject to a number of risks similar to other clinical stage biopharmaceutical companies, including, but not limited to, changes in any of the following areas that the Company believes could have a material adverse effect on its future financial position or results of operations: risks related to the successful discovery and development of its drug candidates, ability to raise additional capital, development of new technological innovations by its competitors and delay or inability to obtain drug substance and finished drug product from the Company's third-party contract manufacturers necessary for the Company's drug candidates, including due to the impact of the current coronavirus (COVID-19) pandemic, protection of intellectual property rights, litigation or claims against the Company based on intellectual property rights and regulatory clearance and market acceptance for any of the Company's products candidates for which the Company receives marketing approval.

Moreover, the Company is subject to risks and uncertainties as a result of the current COVID-19 pandemic and increasing financial market volatility and uncertainty. The COVID-19 pandemic, including the resurgence of cases relating to the spread of new variants, is impacting worldwide economic activity and poses the risk that the Company or its employees, contractors, suppliers and other partners may be prevented from conducting business activities for an indefinite period of time, including due to shutdowns that may be requested or mandated by governmental authorities. The extent to which the COVID-19 pandemic and increasing financial market volatility and uncertainty will impact the Company's business will depend on future developments that are highly uncertain and cannot be predicted at this time.

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. The extent to which the COVID-19 pandemic and the increasing financial market volatility and uncertainty may directly or indirectly impact the Company's financial statements is highly uncertain and subject to change. Management considered the potential impact of the COVID-19 pandemic on its estimates and assumptions and there was not a material impact to the Company's condensed consolidated financial statements as of and for the three and nine months ended August 31, 2022; however, actual results could differ from those estimates and there may be changes to management's estimates in future periods.

The Company relies on single source manufacturers and suppliers for the supply of its drug candidates. Disruption from these manufacturers or suppliers would have a negative impact on the Company's business, financial position and results of operations.

Leases

The Company determines if an arrangement contains a lease at inception. Lease right-of-use (ROU) assets, current lease liabilities and long-term lease liabilities are recognized at the lease commencement date based on the present value of the future minimum lease payments over the lease term at the commencement date. ROU assets also include any initial direct costs incurred and any lease payments made on or before the lease commencement date, less lease incentives received. The Company uses its incremental borrowing rate based on the information available at the commencement date in determining the lease liabilities as the Company's leases generally do not provide an implicit rate. The incremental borrowing rate, the ROU asset and the lease liability are reevaluated upon a lease modification. The Company determines its incremental borrowing rate based on the rate of interest that the Company would have to pay to borrow on a collateralized basis over a similar term, in an amount equal to the lease payments in a similar economic environment. Lease terms may include options to extend or terminate the lease when the Company is reasonably certain that the option will be exercised. Lease expense for operating leases is recognized on a straight-line basis over the lease term. The Company does not have any finance leases.

The Company elected to apply each of the practical expedients described in Topic 842 which allow companies (i) not to reassess prior conclusions on whether any expired or existing contracts are or contain a lease, lease classification, and initial direct costs, (ii) combine lease and non-lease components for all underlying assets groups, and (iii) not recognize ROU assets or lease liabilities for short-term leases. A short-term lease is a lease that, at the commencement date, has a lease term of 12 months or less and does not include an option to purchase the underlying asset that the lessee is reasonably certain to exercise.

Revenue Recognition

The Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To recognize revenue from a contract with a customer, the Company performs the following five steps:

(i) identify the contract(s) with a customer;

(ii) identify the performance obligations in the contract;

(iii) determine the transaction price;

(iv) allocate the transaction price to the performance obligations in the contract; and

(v) recognize revenue when (or as) the Company satisfies a performance obligation.

At contract inception, the Company assesses the goods or services promised within each contract, whether each promised good or service is distinct, and determines those that are performance obligations. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when or as the performance obligation is satisfied.

The Company enters into collaboration agreements under which it may obtain upfront payments, milestone payments, royalty payments and other fees. Promises under these arrangements may include research licenses, research services, including selection campaign research services for certain replacement targets, the obligation to share information during the research and the participation of alliance managers and in joint research committees, joint patent committees and joint steering committees. The Company assesses these promises within the context of the agreements to determine the performance obligations.

Research and collaboration licenses: If a license is determined to be distinct from the other promises identified in the arrangement, the Company recognizes revenue from upfront payments allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring proportional performance for purposes of recognizing revenue from non-refundable, upfront payments. The Company evaluates the measure of proportional performance each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone payments: At the inception of each arrangement that includes research, development, or regulatory milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price. The Company uses the most likely amount method for research, development and regulatory milestone payments. Under the most likely amount method, an entity considers the single most likely amount in a range of possible consideration amounts. If it is probable that a significant revenue reversal would not occur, the associated milestone amount is included in the transaction price.

Sales-based milestones and royalties: For arrangements that include sales-based milestone or royalty payments based on the level of sales, and in which the license is deemed to be the predominant item to which the sales-based milestone or royalties relate to, the Company recognizes revenue in the period in which the sales-based milestone is achieved and in the period in which the sales associated with the royalty occur. To date, the Company has not recognized any sales-based milestone or royalty revenue resulting from its collaboration arrangements.

Customer options: Customer options, such as options granted to allow a licensee to extend a license or research term, to select additional research targets or to choose to research, develop and commercialize licensed compounds are evaluated at contract inception to determine whether those options provide a material right (i.e., an optional good or service offered for free or at a discount) to the customer. If the customer options represent a material right, the material right is treated as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on the standalone selling price. As a practical alternative to estimating the standalone selling price of a material right when the underlying goods or services are both (i) similar to the original goods or services in the contract and (ii) provided in accordance with the terms of the original contract, the Company allocates the total amount of consideration expected to be received from the customer to the total goods or services expected to be provided to the customer. Amounts allocated to any material right are recognized as revenue when or as the related future goods or services are transferred or when the option expires.

Deferred revenue, which is a contract liability, represents net amounts received by the Company for which the related revenues have not been recognized because one or more of the revenue recognition criteria have not been met. The current portion of deferred revenue represents the amount to be recognized within one year from the condensed consolidated balance sheet date based on the estimated performance period of the underlying performance obligation. The noncurrent portion of deferred revenue represents amounts to be recognized after one year through the end of the performance period of the performance obligation.

Recently Adopted Accounting Pronouncements

In December 2019, the Financial Accounting Standards Board (FASB) issued Accounting Standard Update (ASU) No. 2019-12, *Income Taxes (Topic 740)—Simplifying the Accounting for Income Taxes* (ASU 2019-12), which is intended to simplify accounting for income taxes and eliminate certain exceptions from Topic 740 related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. ASU 2019-12 also requires the amount of tax that is based on income to be accounted for under Topic 740 as an income-based tax, with any incremental amount accounted for as a non-income-based tax recognized entirely in the period incurred. The Company adopted ASU 2019-12 as of December 1, 2021 using the modified retrospective method, and recognized an immaterial non-income-based tax within operating expenses in the current period. The adoption had no other impact on the Company's condensed consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)* (ASU 2016-02), which requires the lessee to recognize a ROU asset and a lease liability for operating leases, initially measured at the present value of lease payments, in its consolidated balance sheet. On November 30, 2021, the Company adopted ASU 2016-02 using the alternative modified transition method effective as of December 1, 2020. As a result, the Company has retrospectively changed its previously issued condensed consolidated financial statements as of August 31, 2021 and for the three and nine months ended August 31, 2021 as presented in its August 31, 2021 Quarterly Report on Form 10-Q to reflect the adoption of Topic 842 on December 1, 2020. The condensed consolidated financial statements for the three and nine months ended August 31, 2021 presented herein differ from the Company's condensed consolidated financial statements included in its August 31, 2021 Quarterly Report on Form 10-Q, as those financial statements were prepared using the former accounting standard referred to as ASC Topic 840, *Leases*.

The following table summarizes the effect of the adoption of Topic 842 on the condensed consolidated balance sheet as of December 1, 2020 (in thousands):

	As Previously Reported	Impact of Topic 842 Adoption	As Adjusted
Assets			
Operating lease right-of-use assets	$ —	$ 13,343	$ 13,343
Liabilities			
Operating lease liabilities, current	—	3,342	3,342
Operating lease liabilities, net of current portion	—	10,903	10,903
Accrued and other current liabilities	8,328	(52)	8,276
Other long-term liabilities	$ 850	$ (850)	$ —

The following table summarizes the effect of the adoption of Topic 842 on the condensed consolidated statement of cash flows for the nine months ended August 31, 2021 (in thousands):

	As Previously Reported	Impact of Topic 842 Adoption	As Adjusted
Cash flows from operating activities			
Adjustments to reconcile net loss to net cash used in operating activities:			
Amortization of operating lease right-of-use assets	$ —	$ 2,439	$ 2,439
Changes in operating assets and liabilities:			
Operating lease liabilities	—	(2,432)	(2,432)
Accrued expenses and other liabilities	$ 2,844	$ (7)	$ 2,837

3. Collaboration Agreements

Gilead

In June 2019, the Company entered into a global strategic collaboration agreement with Gilead, which was amended in August 2019 (the Gilead Agreement), to discover, develop and commercialize a pipeline of targeted protein degradation drugs for patients with cancer and other challenging diseases using the Company's DELigase platform to identify novel agents that utilize E3 ligases to induce degradation of five specified drug targets. Under the Gilead Agreement, Gilead has the option to license drug candidates directed to up to five targets resulting from the collaboration and is responsible for the clinical development and commercialization of drug candidates resulting from the collaboration. The Company retains the option to co-develop and co-promote, under a profit share structure, up to two drug candidates in the United States under certain conditions and subject to certain limitations. The collaboration excludes the Company's current internal protein degradation programs for which the Company retains all rights, and also excludes the Company's future internal programs, provided that the Company has distinguished future programs as excluded from the scope of the collaboration. In August 2019 and September 2022, the Company entered into a first amendment and a second amendment, respectively, to the collaboration agreement with Gilead to clarify certain language of the Gilead Agreement. These amendments had no impact on revenue recognition.

Upon signing the Gilead Agreement, Gilead paid the Company an upfront payment of $45.0 million plus $3.0 million in additional fees. In addition, from the signing of the Gilead Agreement to August 31, 2022, the Company has received payments of $32.0 million for research milestones and additional payments. Additionally, the Company recognized a research milestone in August 2022 and anticipates a payment of $2.5 million in the fourth fiscal quarter of 2022. As of August 31, 2022, the Company is eligible to receive up to approximately $2.3 billion in total additional payments based on certain additional fees, payments and the successful completion of certain preclinical, clinical, development and sales milestones. In addition, the Company is eligible to receive tiered royalties from mid-single digit to low tens percentages on annual net sales from any commercial products directed to the optioned collaboration targets, subject to certain reductions and excluding sales in the United States of any products for which the Company exercises its option to co-develop and co-promote, for which the Company and Gilead share profits and losses evenly.

The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. The Company determined that the transaction price at the inception of the Gilead Agreement consisted of the upfront payment of $45.0 million and $3.0 million in additional fees. Upon the achievement of research milestones and additional fees related to target reservations, $34.5 million in variable consideration, which includes $2.5 million added during the three months ended August 31, 2022, was added to the transaction price, and a cumulative effect was recorded as revenue in the period the transaction price increased. The transaction price is recognized as collaboration revenue using the cost-based input method over the estimated contract term of five years.

For the three and nine months ended August 31, 2022, the Company recognized collaboration revenue related to the Gilead Agreement of $7.2 million and $19.5 million, respectively, of which $5.6 million and $14.3 million, respectively, was included in deferred revenue as of November 30, 2021, and $0.6 million and $4.1 million, respectively, was related to activities satisfied in previous periods. For the three and nine months ended August 31, 2021, the Company recognized collaboration revenue related to the Gilead Agreement of $6.1 million and $12.5 million, respectively, of which $4.0 million and $9.6 million, respectively, was included in deferred revenue as of November 30, 2020, and $1.2 million and $1.9 million, respectively, was related to activities satisfied in previous periods. As of August 31, 2022, deferred revenue related to the Gilead Agreement was $29.1 million, of which $15.9 million was current and includes $2.5 million in contract assets representing the unbilled amount related to the research milestone recognized in August 2022. As of November 30, 2021, deferred revenue related to the Gilead Agreement was $41.1 million, of which $19.9 million was current. Additionally, as of November 30, 2021, $6.0 million was recorded in accounts receivable representing the billed amount related to the research milestones recognized in November 2021.

Sanofi

In December 2019, the Company entered into a strategic collaboration with Genzyme Corporation, a subsidiary of Sanofi, which became effective in January 2020 (as subsequently expanded and amended, the Sanofi Agreement), to discover, develop and commercialize a pipeline of targeted protein degradation drugs for patients with challenging diseases in multiple therapeutic areas using the Company's DELigase platform to identify small molecules designed to induce degradation of three specified initial drug targets. In January 2021, as part of the existing collaboration agreement, Sanofi paid the Company $22.0 million to exercise its option to expand the number of targets in the collaboration agreement from three to a total of five targets. In January 2021, the Company and Sanofi entered into a first amendment to the collaboration agreement to modify the research term on all targets (the First Sanofi Amendment). Over time and subject to certain limitations, Sanofi may elect to replace the drug targets with other reserved targets. In December 2021, the Company and Sanofi entered into a second amendment to extend the substitution deadline on certain targets. Under the Sanofi Agreement, Sanofi has exclusive rights and is responsible for the clinical development, commercialization and manufacture of drug candidates resulting from the collaboration, while the Company retains the option to co-develop, co-promote and co-commercialize up to two targets, subject to certain conditions and limitations. In July 2022, the Company entered into a third amendment to further extend the substitution deadline on certain targets. The extensions of the substitution deadline had no impact on revenue recognition. Also in July 2022, Sanofi elected to replace certain drug targets, and the substitution extended the research term of those targets by one year to 5.25 years and increased overall forecasted costs, which had an immaterial impact on revenue recognition. In August 2022, the Company entered into a fourth amendment to modify the research plan for a certain target, which had no impact on revenue recognition.

Upon signing the Sanofi Agreement, Sanofi paid the Company an upfront payment of $55.0 million. Subsequently, in January 2021, Sanofi paid the Company an additional $22.0 million to exercise its option to expand the number of targets beyond the initial targets included in the collaboration. In addition, from the signing of the Sanofi Agreement to August 31, 2022, the Company has received payments of $3.0 million for research milestones. As of August 31, 2022, the Company is eligible to receive up to approximately $2.5 billion in total additional payments based on certain additional fees, payments and the successful completion of certain research development, regulatory and sales milestones, as well as tiered royalties ranging from mid-single digit to low teen percentages on annual net sales of any commercial products that may result from the collaboration, subject to certain reductions and excluding sales in the United States of any products for which the Company exercises its option to co-develop and co-promote, for which the parties share profits and losses evenly.

The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. At the inception of the Sanofi Agreement, the Company determined that the transaction price consisted of the upfront payment of $55.0 million for three initial drug targets and $22.0 million for two additional targets. Subsequently, upon the achievement of research milestones, $3.0 million in variable consideration was added to the transaction price, and a cumulative effect was recorded as revenue in the period the transaction price increased. Revenue is recognized using the cost-based input method over the research term of 4.25 years, the revised research period that was agreed to in January 2021 in the First Sanofi Amendment for certain targets, and 5.25 years, the revised research period due to the target substitutions in July 2022, for certain other targets.

For the three and nine months ended August 31, 2022, the Company recognized collaboration revenue related to the Sanofi Agreement of $3.6 million and $12.4 million, respectively, of which $3.6 million and $11.8 million, respectively, was included in deferred revenue as of November 30, 2021 and zero and $0.4 million, respectively, was related to activities satisfied in previous periods. For the three and nine months ended August 31, 2021, the Company recognized collaboration revenue related to the Sanofi Agreement of $4.2 million and $9.8 million, respectively, of which $4.0 million and $9.6 million, respectively, was included in deferred revenue as of November 30, 2020. As of August 31, 2022 and November 30, 2021, deferred revenue related to the Sanofi Agreement was $48.8 million, of which $20.5 million was current, and $59.2 million, of which $21.3 million was current, respectively.

4. Condensed Consolidated Balance Sheet Components

Property and Equipment, Net

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

	August 31, 2022	November 30, 2021
Laboratory equipment	$ 25,352	$ 18,321
Leasehold improvements	3,332	3,083
Computer equipment	786	538
Furniture and fixtures	453	437
Software	4,240	3,349
Software in progress	488	491
Total property and equipment, gross	34,651	26,219
Less: Accumulated depreciation and amortization	(18,150)	(14,879)
Total property and equipment, net	$ 16,501	$ 11,340

Depreciation and amortization expense was $1.5 million and $0.7 million for the three months ended August 31, 2022 and 2021, respectively, and $3.7 million and $2.0 million for the nine months ended August 31, 2022 and 2021, respectively. All long-lived assets are maintained in the United States.

Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	August 31, 2022	November 30, 2021
Accrued compensation	$ 10,312	$ 8,854
Accrued contract research and lab supplies	6,267	4,158
Accrued professional services	1,335	803
Accrued taxes	41	75
Other	1,654	659
Total accrued expenses and other current liabilities	$ 19,609	$ 14,549

5. Fair Value Measurements

In accordance with the authoritative guidance on fair value measurements and disclosures under U.S. GAAP, the Company discloses and recognizes the fair value of its assets and liabilities using a hierarchy that prioritizes the inputs to valuation techniques used to measure fair value. The hierarchy gives the highest priority to valuations based upon unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 measurements) and the lowest priority to valuations based upon unobservable inputs that are significant to the valuation (Level 3 measurements). The guidance establishes three levels of the fair value hierarchy as follows:

Level 1—Inputs that reflect unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date;

Level 2—Inputs other than quoted prices included within Level 1 that are observable for the asset or liability either directly or indirectly, including inputs in markets that are not considered to be active; and

Level 3—Inputs that are unobservable.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company’s assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and considers factors specific to the asset or liability.

The following tables present the Company's investments, which consist of cash equivalents and available-for-sale marketable securities, that are measured at fair value on a recurring basis as of August 31, 2022 and November 30, 2021 (in thousands):

August 31, 2022	Level	Amortized cost	Unrealized gain	Unrealized loss	Estimated fair value
Money market funds	Level 1	$ 44,738	$ —	$ —	$ 44,738
U.S. treasury securities	Level 1	90,301	—	(1,067)	89,234
Corporate debt securities	Level 2	87,289	—	(1,081)	86,208
U.S. government agency securities	Level 2	19,497	—	(171)	19,326
Corporate commercial paper	Level 2	85,539	—	—	85,539
Foreign government securities	Level 2	12,103	—	(137)	11,966
Municipal securities	Level 2	4,655	—	(6)	4,649
Long-term marketable securities:					
U.S. treasury securities	Level 1	5,734	—	(16)	5,718
Corporate debt securities	Level 2	14,854	—	(553)	14,301
U.S. government agency securities	Level 2	49,816	4	(714)	49,106
Total		$ 414,526	$ 4	$ (3,745)	$ 410,785
Included in Cash and cash equivalents		$ 44,738	$ —	$ —	$ 44,738
Included in Short-term marketable securities		$ 299,384	$ —	$ (2,462)	$ 296,922
Included in Long-term marketable securities		$ 70,404	$ 4	$ (1,283)	$ 69,125

November 30, 2021	Level	Amortized cost	Unrealized gain	Unrealized loss	Estimated fair value
Money market funds	Level 1	$ 73,438	$ —	$ —	$ 73,438
U.S. treasury securities	Level 1	20,608	—	(9)	20,599
Corporate debt securities	Level 2	46,599	1	(54)	46,546
U.S. government agency securities	Level 2	16,496	1	(14)	16,483
Corporate commercial paper	Level 2	121,495	—	—	121,495
Municipal securities	Level 2	10,082	9	—	10,091
Long-term marketable securities:					
U.S. treasury securities	Level 1	39,932	—	(85)	39,847
Corporate debt securities	Level 2	74,334	—	(365)	73,969
U.S. government agency securities	Level 2	16,236	—	(67)	16,169
Municipal securities	Level 2	7,229	—	(25)	7,204
Total		$ 426,449	$ 11	$ (619)	$ 425,841
Included in Cash and cash equivalents		$ 73,438	$ —	$ —	$ 73,438
Included in Short-term marketable securities		$ 215,280	$ 11	$ (77)	$ 215,214
Included in Long-term marketable securities		$ 137,731	$ —	$ (542)	$ 137,189

The accrued interest receivable related to the Company's marketable securities was $1.1 million and $0.9 million as of August 31, 2022 and November 30, 2021, respectively, and was included in prepaid expenses and other current assets on the condensed consolidated balance sheet.

The Company classifies its money market funds and U.S. treasury securities, which are valued based on quoted market prices in active markets with no valuation adjustment, as Level 1 assets within the fair value hierarchy.

The Company classifies its marketable securities in corporate debt securities, U.S. government agency securities, corporate commercial paper, foreign government securities and municipal securities as Level 2 assets within the fair value hierarchy. The fair values of these marketable securities are estimated by taking into consideration valuations obtained from third-party pricing services. The pricing services utilize industry standard valuation models, including both income- and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar securities, issuer credit spreads, benchmark securities, prepayment/default projections based on historical data and other observable inputs. There were no transfers of financial instruments between valuation levels during the three and nine months ended August 31, 2022 and 2021.

As of August 31, 2022 and November 30, 2021, the unrealized losses for available-for-sale securities were non-credit related, and the Company does not intend to sell the securities that were in an unrealized loss position, nor will it be required to sell those securities before recovery of their amortized cost basis, which may be maturity. As of August 31, 2022 and November 30, 2021, no allowance for credit losses for the Company's marketable securities was recorded. During the three and nine months ended August 31, 2022 and 2021, the Company did not recognize any impairment losses related to marketable securities.

6. Commitments and Contingencies

Legal Proceedings

From time to time, the Company may be involved in legal proceedings in the ordinary course of business. The Company accrues a liability for such matters when it is probable that future expenditures will be made and that such expenditures can be reasonably estimated. Significant judgment is required to determine both probability and the estimated amount. Legal fees and other costs associated with such actions are expensed as incurred. As of August 31, 2022, the Company was not a party to any material legal proceedings.

Indemnifications

In the ordinary course of business, the Company often includes standard indemnification provisions in its arrangements with its partners, suppliers and vendors, among others. Pursuant to these provisions, the Company may be obligated to indemnify such parties for losses or claims suffered or incurred in connection with its service, breach of representations or covenants, intellectual property infringement or other claims made against such parties. These provisions may limit the time within which an indemnification claim can be made. It is not possible to determine the maximum potential amount under these indemnification obligations due to the limited history of prior indemnification claims and the unique facts and circumstances involved in each particular agreement. The Company has not incurred any material costs as a result of such indemnifications and has not accrued any liabilities related to such obligations in these condensed consolidated financial statements as management believes such liability is immaterial.

In addition, the Company has entered into indemnification agreements with directors and certain officers and employees that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors, officers or employees. No demands have been made upon the Company to provide indemnification under such agreements, and thus, there are no claims that the Company is aware of that could have a material effect on the Company's condensed consolidated financial statements. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is not specified in the agreements. However, the Company currently has directors' and officers' insurance that reduces its exposure and may enable the Company to recover a portion of any future amounts paid.

Operating Leases

The Company leases office and laboratory facilities within the same building in San Francisco, California under several lease agreements. The terms of these lease agreements expire on April 30, 2025.

In July 2021, the Company entered into a lease agreement for the lease of approximately 19,320 square feet of office space in San Francisco, California, for a research and development laboratory and related uses. The lease commenced on December 1, 2021 and will expire on June 30, 2024, unless terminated earlier.

In March 2022, the Company entered into a lease agreement for the lease of approximately 46,434 square feet of office space in The Woodlands, Texas, for a research and development laboratory and related uses. The Company obtained access to the premise on August 1, 2022, and the lease is expected to commence in fiscal year 2023 when the underlying assets become available for use and will expire on March 1, 2035, unless terminated earlier. The minimum rent payable by the Company under the lease will be approximately $205,000 per month, beginning on March 1, 2023, which amount will increase by 3% per year over the term of the lease; provided that, for the period between March 1, 2023 and February 29, 2024, the minimum rent payable by the Company under the lease will be approximately $154,000 per month. The Company will also be responsible for the payment of additional rent to cover the Company's share of the annual operating and tax expenses and utilities costs for the building.

Operating lease expenses, excluding additional rent charges for utilities, maintenance and real estate taxes, were $1.5 million and $0.9 million for the three months ended August 31, 2022 and 2021, respectively, and $4.4 million and $2.6 million for the nine months ended August 31, 2022 and 2021, respectively. Short-term lease expense was not material for all periods presented.

Other information related to leases were as follows (in thousands):

	Nine Months Ended August 31,	
	2022	2021
Cash paid for amounts included in the measurement of lease liabilities:		
Cash flows from operating leases	$ 5,198	$ 2,784
Supplemental disclosures of non-cash investing and financing activities:		
Right-of-use assets recognized in exchange for lease obligations	$ 5,060	$ 2,097

The undiscounted future non-cancellable lease payments under the Company's lease agreements as of August 31, 2022 were as follows (in thousands):

Year ending November 30,	Operating Leases
2022 (remaining 3 months)	$ 1,376
2023	6,976
2024	7,422
2025	4,330
2026	2,670
2027	2,750
2028 to 2035	22,556
Total undiscounted lease payments	48,080
Less: imputed interest	(525)
Less: undiscounted lease payments related to the lease in The Woodlands, Texas	(34,314)
Total lease liabilities	$ 13,241
Operating lease current liabilities	$ 5,496
Operating lease long-term liabilities	7,745
Total lease liabilities	$ 13,241

7. Common Stock

The Company's Restated Certificate of Incorporation authorizes the Company to issue up to 500,000,000 shares of common stock, $0.001 par value per share, as of August 31, 2022 and November 30, 2021. Holders of common stock are entitled to dividends when and if declared by the Company's board of directors, subject to the prior rights of the holders of shares of preferred stock. The holder of each share of common stock is entitled to one vote. As of August 31, 2022, no dividends have been declared.

In July 2022, the Company issued pre-funded warrants to purchase an aggregate of 6,814,920 shares of the Company's common stock in RDOs at a price of $13.939 per pre-funded warrant. The pre-funded warrants were immediately exercisable, have an exercise price of $0.001 and may be exercised at any time after the date of issuance. A holder of pre-funded warrants may not exercise the warrant if the holder, together with its affiliates, would beneficially own more than 9.99% of the number of shares of the Company's common stock outstanding immediately after giving effect to such exercise. A holder of the pre-funded warrants may increase or decrease this percentage not in excess of 19.99% by providing at least 61 days' prior notice to the Company. As of August 31, 2022, all of the pre-funded warrants remained available for exercise.

The pre-funded warrants were classified as a component of permanent equity in the Company's condensed consolidated balance sheet as they are freestanding financial instruments that are immediately exercisable, do not embody an obligation for the Company to repurchase its own shares and permit the holders to receive a fixed number of shares of common stock upon exercise. All of the shares underlying the pre-funded warrants have been included in the weighted-average number of shares of common stock used to calculate net loss per share attributable to common stockholders because the shares may be issued for little or no consideration, are fully vested and are exercisable after the original issuance date of the pre-funded warrants.

Common stock reserved for future issuance, on an as-if converted basis, as of August 31, 2022 and November 30, 2021, consists of the following:

	August 31, 2022	November 30, 2021
Options under stock option plan issued and outstanding	8,115,201	5,878,552
Shares available for future stock option grants	1,031,871	2,562,570
Shares available for issuance under employee stock purchase plan	1,325,523	1,015,184
Restricted stock units issued and outstanding	753,518	20,000
Pre-funded warrants issued and outstanding	6,814,920	—
Total common stock reserved for future issuance	18,041,033	9,476,306

8. Stock-Based Compensation

Equity Incentive Plans

The Company's 2020 Equity Incentive Plan (the 2020 Plan) serves as the successor to the Company's 2012 Equity Incentive Plan (together with the 2020 Plan, the Stock Plans) and provides for the granting of stock options, stock appreciation rights, restricted stock awards, restricted stock units (RSUs), performance awards and stock bonus awards to employees, directors, consultants, independent contractors and advisors of the Company.

Option activity under the Stock Plans is set forth below:

	Number of options outstanding	Weighted-average exercise price	Weighted-average contractual life (in years)	Aggregate intrinsic value(1) (in thousands)
Balances as of November 30, 2021	5,878,552	$ 19.42	8.67	$ 65,692
Options granted	3,000,206	18.28		
Options exercised	(315,172)	3.27		
Options forfeited	(448,385)	20.27		
Balances as of August 31, 2022	8,115,201	$ 19.58	8.65	$ 20,921
Options vested and expected to vest as of August 31, 2022(2)	8,142,625	$ 19.54	8.65	$ 21,159
Options exercisable as of August 31, 2022	3,195,076	$ 14.79	7.72	$ 19,159

(1) The aggregate intrinsic values were calculated as the pre-tax difference between the exercise price of stock options and the quoted market price of the Company's common stock on August 31, 2022 for all in-the-money stock options.

(2) Certain stock options granted by the Company prior to the date of IPO are exercisable at the date of grant, with unvested shares subject to repurchase by the Company in the event of a voluntary or involuntary termination of employment of the stockholder. Such exercises are recorded as a liability in the condensed consolidated balance sheets and reclassified into equity as the options vest. As of August 31, 2022, a total of 27,424 shares of common stock were subject to repurchase by the Company at the lower of (i) the fair market value of such shares on the date of repurchase, or (ii) the original exercise price of such shares. The corresponding exercise value of $0.2 million as of August 31, 2022 is recorded in share-based compensation liability.

RSU activity under the Stock Plans is set forth below:

	Number of RSUs	Weighted-average grant date fair value
Balances as of November 30, 2021	20,000	$ 27.42
RSUs granted	797,282	19.56
RSUs vested	(31,934)	20.73
RSUs forfeited	(31,830)	23.11
Balances as of August 31, 2022	753,518	$ 19.57

Employee Stock Purchase Plan

Under the Company's 2020 Employee Stock Purchase Plan (the ESPP), eligible employees are entitled to purchase shares of common stock with accumulated payroll deductions. During the nine months ended August 31, 2022, the Company issued 136,304 shares pursuant to the ESPP at a weighted-average price of $14.34 per share.

Stock-Based Compensation

Stock-based compensation expense related to the Stock Plans and the ESPP that is included in the Company's condensed consolidated statements of operations is as follows (in thousands):

	Three Months Ended, August 31,		Nine Months Ended, August 31,	
	2022	2021	2022	2021
Research and development	$ 4,229	$ 2,212	$ 11,766	$ 5,450
General and administrative	2,759	2,101	8,068	5,507
Total stock-based compensation	$ 6,988	$ 4,313	$ 19,834	$ 10,957

As of August 31, 2022, the total compensation cost related to stock-based awards not yet recognized was $85.9 million, which is expected to be amortized on a straight-line basis over the weighted-average remaining vesting period of approximately 2.9 years.

9. Defined Contribution Plan

The Company sponsors a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code of 1986, as amended (the 401(k) Plan), which provides for the Company to make discretionary matching or discretionary annual contributions to the 401(k) Plan, for its employees. Substantially all of the Company's employees are eligible to participate. Employees may contribute a percentage of their annual compensation to the plan, subject to statutory limitations. The Company has made contributions to the 401(k) Plan and recorded contribution expense of $0.1 million and $0.1 million during the three months ended August 31, 2022 and 2021, respectively, and $0.8 million and $0.5 million during the nine months ended August 31, 2022 and 2021, respectively.

10. Income Taxes

For the three and nine months ended August 31, 2022, the Company did not record any current income tax expense or provision and for the three and nine months ended August 31, 2021, the Company recorded a current income tax benefit of $0.1 million and an expense of $0.1 million, respectively. Deferred income taxes reflect the net tax effects of loss and credit carryforwards and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Realization of the deferred tax assets is dependent upon future taxable income, the amount, if any, and timing of which are uncertain. The Company has generated losses since inception and has established a valuation allowance to offset deferred tax assets as of August 31, 2022 and 2021 due to the uncertainty of realizing future tax benefits from its net operating loss carryforwards and other deferred tax assets.

In August 2022, the U.S. Inflation Reduction Act (the Act) was enacted into law. The Act includes various tax provisions, including an excise tax on stock repurchases, expanded tax credits for clean energy incentives and a corporate alternative minimum tax that generally applies to U.S. corporations with adjusted financial statement income in excess of $1.0 billion. The Company does not expect the Act to have a material impact on its financial statements.

In January 2019, the California Franchise Tax Board (the FTB) commenced an examination of the Company's California income tax returns for the tax years ending in 2015, 2016, 2017 and 2018. During the year ended November 30, 2021, the FTB issued proposed audit assessments related to revenue sourcing and R&D credits. The Company does not agree with the FTB assessments and intends to challenge the assessments. Pursuant to a measurement analysis, the Company has not recorded an unrecognized tax benefit related to the FTB's sourcing position. The Company maintains an unrecognized tax benefit related to its California R&D credits for all years.

11. Net Loss Per Share

The following table sets forth the computation of the Company's basic and diluted net loss per share attributable to common stockholders, which excludes shares which are legally outstanding but subject to repurchase by the Company (in thousands, except share and per share data):

	Three Months Ended August 31,		Nine Months Ended August 31,	
	2022	2021	2022	2021
Numerator:				
Net loss	$ (45,709)	$ (28,835)	$ (133,643)	$ (79,492)
Denominator:				
Weighted-average number of shares outstanding, basic and diluted(1)	50,868,542	44,374,389	46,835,776	42,344,420
Net loss per share, basic and diluted	$ (0.90)	$ (0.65)	$ (2.85)	$ (1.88)

(1) The shares underlying the pre-funded warrants to purchase an aggregate of 6,814,920 shares of the Company's common stock have been included in the calculation of the weighted-average number of shares outstanding, basic and diluted, for the three and nine months ended August 31, 2022.

The following potentially dilutive securities were excluded from the computation of the diluted net loss per share of common stock for the periods presented because their effect would have been anti-dilutive:

	August 31,	
	2022	2021
Options to purchase common stock	8,115,201	5,593,412
Options early exercised subject to vesting	27,424	76,175
Shares expected to be purchased under employee stock purchase plan	123,194	43,274
Restricted stock	753,518	20,000
Total	9,019,337	5,732,861

12. Related Party Transactions

The Company's Chief Financial Officer is a trustee for the Company's healthcare plan provider. Expenses related to the healthcare plan premiums were $1.0 million and $0.7 million for the three months ended August 31, 2022 and 2021, respectively, and $2.9 million and $1.8 million for the nine months ended August 31, 2022 and 2021, respectively. As of August 31, 2022 and November 30, 2021, the amount recorded in accrued liabilities and accounts payable in connection with this healthcare plan provider was not material.

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with (1) the unaudited condensed consolidated financial statements and the related notes included in Part I, Item 1 of this Quarterly Report on Form 10-Q and (2) the audited consolidated financial statements and related notes and management's discussion and analysis of financial condition and results of operations for the fiscal year ended November 30, 2021 included in our Annual Report on Form 10-K filed on January 28, 2022 (2021 Form 10-K). As discussed in the section titled "Special Note Regarding Forward Looking Statements," the following discussion and analysis contains forward looking statements that involve risks and uncertainties, as well as assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward looking statements. Factors that could cause or contribute to these differences include, but are not limited to, those identified below and those discussed in the section titled "Risk Factors" in Part II, Item 1A of this Quarterly Report on Form 10-Q.

Overview

We are a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of small molecule and cell therapies based on the modulation of cellular protein levels as a novel treatment approach for cancer and other challenging diseases. Leveraging our extensive expertise in E3 ligases together with our proprietary DNA-encoded libraries, we have built DELigase, an integrated discovery platform to identify and advance novel drug candidates targeting E3 ligases, a broad class of enzymes that can modulate proteins within the cell. Targeted Protein Modulation, our drug discovery approach, either harnesses or inhibits the natural function of E3 ligases within the ubiquitin-proteasome system to selectively decrease or increase cellular protein levels to treat disease. Our wholly owned pipeline comprises four clinical stage drug candidates in our Targeted Protein Degradation and Targeted Protein Elevation portfolios.

Targeted Protein Degradation:

Our portfolio of targeted protein degraders of Bruton's tyrosine kinase (BTK), a B-cell signaling protein, comprises NX-2127, an orally bioavailable BTK degrader for the treatment of relapsed or refractory B-cell malignancies, and NX-5948, an orally bioavailable BTK degrader for the treatment of relapsed or refractory B-cell malignancies and potentially autoimmune diseases.

NX-2127: We are currently enrolling patients in a Phase 1a/1b dose-escalation and cohort expansion study in patients with relapsed or refractory B-cell malignancies. We have initiated the first of several potential Phase 1b expansion cohorts for patients with relapsed chronic lymphocytic leukemia, and enrollment continues in the Phase 1a dose-escalation portion of the trial for patients with several types of non-Hodgkin lymphoma.

NX-5948: We are currently enrolling patients in the Phase 1a portion of a Phase 1a/1b dose-escalation and cohort expansion study in patients with relapsed or refractory B-cell malignancies.

Targeted Protein Elevation:

Our portfolio of inhibitors of Casitas B-lineage lymphoma proto-oncogene B (CBL-B), an E3 ligase that regulates the activation of multiple immune cell types including T cells and NK cells, comprises NX-1607, an orally bioavailable CBL-B inhibitor for immuno-oncology indications and for which we were awarded an Innovative Passport from the UK Medicines and Healthcare products Regulatory Agency to accelerate time to market and facilitate patient access to novel drugs to treat serious and life-threatening diseases, and NX-0255, for ex vivo use to enhance adoptive T-cell therapy including our drug-enhanced tumor infiltrating lymphocyte (TIL) therapy, DeTIL-0255.

NX-1607: We are currently enrolling patients in the Phase 1a portion of a Phase 1a/1b dose-escalation and cohort expansion study in patients with solid tumors and lymphomas.

DeTIL-0255: We are currently enrolling patients in the Phase 1 clinical trial for our first cell therapy candidate, DeTIL-0255, in patients with gynecologic cancers including ovarian cancer, endometrial cancer, and cervical cancer.

Preclinical programs:

Beyond our clinical candidates, we are advancing additional wholly owned and partnered preclinical programs within our core therapeutic focus in cancer and selectively in non-oncology therapeutic areas. Our pipeline includes highly validated and classically undruggable targets across our proprietary efforts, academic collaborations and our established strategic collaborations with Sanofi S.A. (Sanofi), and Gilead Sciences, Inc. (Gilead).

Since the commencement of our operations, we have devoted substantially all of our resources to conducting research and development activities, establishing and maintaining our intellectual property portfolio, establishing our corporate infrastructure, raising capital and providing general and administrative support for these operations. We have funded our operations to date primarily from proceeds received under collaboration and license agreements with Sanofi, Gilead, and Celgene Corporation and the issuance and sale of common stock and redeemable convertible preferred stock. We do not expect to generate product revenue unless and until we successfully develop and obtain approval for the commercialization of a drug candidate, and we cannot assure you that we will ever generate significant revenue or profits.

Since inception, we have generally incurred significant losses and negative cash flows from operations. During the nine months ended August 31, 2022 and 2021, we incurred net losses of $133.6 million and $79.5 million, respectively. As of August 31, 2022, we had an accumulated deficit of $354.5 million. These losses have resulted primarily from costs incurred in connection with research and development activities and general and administrative costs associated with our operations.

We do not expect to generate any revenue from commercial product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our drug candidates, which we expect will take a number of years, if ever. We expect our expenses will increase substantially as we advance our drug candidates through preclinical and clinical development; enter advanced clinical development and scale up external manufacturing capabilities to supply clinical trials; apply our DELigase platform to advance additional drug candidates and expand the capabilities of our platform; seek marketing approvals for any drug candidates that successfully complete clinical trials; ultimately establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we may obtain marketing approval; expand, maintain and protect our intellectual property portfolio; and hire additional clinical, regulatory, manufacturing, quality assurance and scientific personnel. Furthermore, we expect to continue to incur additional costs associated with operating as a public company, including significant legal, accounting, insurance, investor relations and other administrative and professional services expenses.

Our net losses and cash flows may fluctuate significantly from period to period, depending on, among other things, variations in the level of expense related to the ongoing development of our drug candidates, our DELigase platform or future development programs; the delay, addition or termination of clinical trials; and the execution of any additional collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under such arrangements.

As of August 31, 2022, we had $413.6 million in cash, cash equivalents and marketable securities. We expect that our existing cash, cash equivalents and marketable securities are sufficient to fund our operations for at least the next 12 months. See the section titled "—Liquidity and Capital Resources" for more information. To finance our operations beyond that point, we will need to raise substantial additional capital to complete the development and commercialization of our drug candidates. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing and distribution arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

We are subject to risks and uncertainties as a result of the current COVID-19 pandemic and increasing financial market volatility and uncertainty. The COVID-19 pandemic, including the resurgence of cases relating to the spread of new variants, is impacting worldwide economic activity and poses the risk that we or our employees, contractors, suppliers and other partners may be prevented from conducting business activities for an indefinite period of time, including due to shutdowns that may be requested or mandated by governmental authorities. While the impact of the COVID-19 pandemic to our current operations has been minimal as we have recently commenced clinical development of our four lead drug candidates, the extent to which the COVID-19 pandemic and increasing financial market volatility and uncertainty will impact our business, financial condition, liquidity, access to capital, and results of operations in the future will depend on future developments that are highly uncertain and cannot be predicted at this time.

Collaborations and License Agreements

Gilead Collaboration, Option and License Agreement

In June 2019, we entered into a global strategic collaboration agreement with Gilead, which was amended in August 2019 (the Gilead Agreement), to discover, develop and commercialize a pipeline of targeted protein degradation drugs for patients with cancer and other challenging diseases using our DELigase platform to identify novel agents that utilize E3 ligases to induce degradation of five specified drug targets. Under the Gilead Agreement, Gilead has the option to license drug candidates directed to up to five targets resulting from the collaboration and is responsible for the clinical development and commercialization of drug candidates resulting from the collaboration. We retain the option to co-develop and co-promote, under a profit share structure, up to two drug candidates in the United States under certain conditions and subject to certain limitations. The collaboration excludes our current internal protein degradation programs for which we retain all rights, and also excludes our future internal programs, provided that we have distinguished future programs as excluded from the scope of the collaboration. In August 2019 and September 2022, we entered into a first amendment and a second amendment, respectively, to the collaboration agreement with Gilead to clarify certain language of the Gilead Agreement. These amendments had no impact on revenue recognition.

Upon signing the Gilead Agreement, Gilead paid us an upfront payment of $45.0 million plus $3.0 million in additional fees. In addition, from the signing of the Gilead Agreement to August 31, 2022, we received payments of $32.0 million for research milestones and additional payments. Additionally, we recognized a research milestone in August 2022 and anticipate a payment of $2.5 million in the fourth fiscal quarter of 2022. As of August 31, 2022, we are eligible to receive up to approximately $2.3 billion in total additional payments based on certain additional fees, payments and the successful completion of certain preclinical, clinical, development and sales milestones. In addition, we are eligible to receive tiered royalties from mid-single digit to low tens percentages on annual net sales from any commercial products directed to the optioned collaboration targets, subject to certain reductions and excluding sales in the United States of any products for which we exercise our option to co-develop and co-promote, for which we share profits and losses evenly.

We recognized collaboration revenue from the Gilead Agreement of $7.2 million and $19.5 million during the three and nine months ended August 31, 2022, respectively, and $6.1 million and $12.5 million during the three and nine months ended August 31, 2021, respectively. As of August 31, 2022 and November 30, 2021, there was $29.1 million and $41.1 million, respectively, of deferred revenue related to payments received and to be received by us under the Gilead Agreement.

Sanofi Collaboration and License Agreement

In December 2019, we entered into a strategic collaboration with Genzyme Corporation, a subsidiary of Sanofi, which became effective in January 2020 (as subsequently expanded and amended, the Sanofi Agreement), to discover, develop and commercialize a pipeline of targeted protein degradation drugs for patients with challenging diseases in multiple therapeutic areas using our DELigase platform to identify small molecules designed to induce degradation of three specified initial drug targets. In January 2021, as part of the existing collaboration, Sanofi paid us $22.0 million to exercise its option to expand the number of targets in the collaboration agreement from three to a total of five targets. Over time and subject to certain limitations, Sanofi may elect to replace the drug targets with other reserved targets. In January 2021, we entered into the First Sanofi Amendment to the collaboration agreement with Sanofi to modify the research term on all targets. In December 2021, we entered into the Second Sanofi Amendment to the collaboration agreement with Sanofi to extend the substitution deadline on certain targets. Under the Sanofi Agreement, Sanofi has exclusive rights and is responsible for the clinical development, commercialization and manufacture of drug candidates resulting from the collaboration, while we retain the option to co-develop, co-promote and co-commercialize all drug candidates in the United States directed to up to two targets under certain conditions, subject to certain conditions and limitations. In July 2022, we entered into the Third Sanofi Amendment to further extend the substitution deadline on certain targets. The extensions of the substitution deadline had no impact on revenue recognition. Also in July 2022, Sanofi elected to replace certain drug targets, and the substitution extended the research term of those targets by one year to 5.25 years and increased overall forecasted costs, which had an immaterial impact on revenue recognition. In August 2022, we entered into the Fourth Sanofi Amendment to modify the research plan for a certain target, which had no impact on revenue recognition.

Upon signing the Sanofi Agreement, Sanofi paid us an upfront payment of $55.0 million. Subsequently, in January 2021, Sanofi paid us an additional $22.0 million to exercise its option to expand the number of targets beyond the initial targets included in the collaboration. In addition, from the signing of the Sanofi Agreement to August 31, 2022, we received payments of $3.0 million for research milestones. As of August 31, 2022, we are eligible to receive up to approximately $2.5 billion in total additional payments based on certain additional fees, payments and the successful completion of certain research development, regulatory and sales milestones, as well as tiered royalties ranging from mid-single digit to low teen percentages on annual net sales of any commercial products that may result from the collaboration, subject to certain reductions and excluding sales in the United States of any products for which we exercise our option to co-develop and co-promote, for which we share profits and losses evenly.

We recognized collaboration revenue from the Sanofi Agreement of $3.6 million and $12.4 million during the three and nine months ended August 31, 2022, respectively, and $4.2 million and $9.8 million during the three and nine months ended August 31, 2021, respectively. As of August 31, 2022 and November 30, 2021, there was $48.8 million and $59.2 million, respectively, of deferred revenue related to payments received by us under the Sanofi Agreement.

Components of Results of Operations

Collaboration Revenue

We have no products approved for commercial sale and to date have not generated any revenue from the sale of products and do not expect to generate any revenue from the sale of products in the near future.

Our revenue to date has been generated from payments received pursuant to collaboration and license arrangements with strategic partners. Collaboration revenue consists of revenue received from upfront, milestone and contingent payments received from our collaborators. We recognize revenue from upfront payments over the contract term using the cost-based input method. The material right to the two additional targets under the Sanofi Agreement was accounted for using the practical alternative and the expected consideration to be received on the options was included for revenue allocation. We expect to continue recognizing revenue from upfront payments related to our collaboration agreements using the cost-based input method in the foreseeable future.

In addition to receiving upfront payments, we may also be entitled to milestones and other contingent payments upon achieving predefined objectives. If a milestone is considered probable of being reached, and if it is probable that a significant revenue reversal would not occur, the associated milestone amount would also be included in the transaction price.

We expect that any collaboration revenue we generate from our current collaboration and license agreements, and from any future collaboration partners, will fluctuate in the future as a result of the timing and amount of upfront, milestones and other collaboration agreement payments and other factors.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the discovery and development of our drug candidates. We expense both internal and external research and development expenses to operations in the periods in which they are incurred. Nonrefundable advance payments for goods or services to be received in future periods for use in research and development activities are deferred and capitalized. The capitalized amounts are then expensed as the related goods are delivered and as services are performed. We track the external research and development costs incurred for each of our drug candidates.

Internal research and development costs include:

- payroll and personnel expenses, including benefits, stock-based compensation and travel expenses, for our research and development functions; and
- depreciation of research and development equipment, allocated overhead and facilities-related expenses.

External research and development expenses consist primarily of costs incurred for the development of our drug candidates and may include:

- fees paid to third parties such as consultants, contractors and contract research organizations to conduct our clinical trials, discovery programs and preclinical studies;
- costs to acquire, develop and manufacture supplies for clinical trials and preclinical studies, including fees paid to third parties such as contract manufacturing organizations; and
- expenses related to laboratory supplies and services.

We expect our research and development expenses to increase substantially for the foreseeable future as we conduct clinical trials for our drug candidates, continue to invest in research and development activities for discovery programs and preclinical studies, pursue regulatory approval of our drug candidates and expand our drug candidate pipeline. The process of conducting the necessary preclinical and clinical research to obtain regulatory approval is costly and time-consuming. To the extent that our drug candidates advance to and continue to advance through clinical trials, our expenses will continue increasing substantially and may become more variable. The actual probability of success for our drug candidates may be affected by a variety of factors, including the safety and efficacy of our drug candidates, investment in our clinical programs, the ability of collaborators to successfully develop our licensed drug candidates, manufacturing capability, competition with other products and commercial viability. As a result of these variables, we are unable to determine when and to what extent we will generate revenue from the commercialization and sale of our drug candidates. We may never succeed in achieving regulatory approval for any of our drug candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of payroll and personnel expenses, including benefits and stock-based compensation, facilities-related expenses and professional fees for legal, consulting and audit and tax services. We expect our general and administrative expenses to increase for the foreseeable future as we continue to improve our infrastructure, increase our headcount and operate as a public company. This may include expenses related to compliance with the rules and regulations of the Securities and Exchange Commission (SEC) and listing standards applicable to companies listed on a national securities exchange, additional insurance, investor relations activities and other administrative and professional services. We also expect our intellectual property expenses to increase as we expand our intellectual property portfolio.

Interest and Other Income, Net

Interest and other income, net primarily consists of interest earned on our cash, cash equivalents and marketable securities. We expect interest income to vary each reporting period depending on our average bank deposit, money market fund, and marketable securities balances during the period and market interest rates.

Provision for Income Taxes

The provision for income taxes primarily consists of reserves for unrecognized tax benefits and state taxes. The benefit for income taxes consists of a discrete tax benefit from an adjustment to the net operating loss (NOL) deferred tax asset and valuation allowance. We have generated NOLs since inception and have established a full valuation allowance against our deferred tax assets due to the uncertainty surrounding the realization of such assets.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our condensed consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles (U.S. GAAP). The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenue generated and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on other relevant assumptions that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our critical accounting policies and more significant areas involving management's judgments and estimates used in preparation of our financial statements are discussed in the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our 2021 Form 10-K. There have been no significant changes to these policies for the three and nine months ended August 31, 2022.

Recent Accounting Pronouncements

See Note 2, "Summary of significant accounting policies—Recent accounting pronouncements" to our condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q for more information.

Results of Operations

Comparison of the three and nine months ended August 31, 2022 and 2021

Our results of operations for the three and nine months ended August 31, 2022 and 2021 are summarized as follows (in thousands):

	Three Months Ended August 31,			Nine Months Ended August 31,		
	2022	2021	Change	2022	2021	Change
Collaboration revenue	$ 10,791	$ 10,252	$ 539	$ 31,844	$ 22,354	$ 9,490
Operating expenses:						
Research and development	47,761	30,906	16,855	138,391	79,903	58,488
General and administrative	9,748	8,343	1,405	28,630	22,384	6,246
Total operating expenses	57,509	39,249	18,260	167,021	102,287	64,734
Loss from operations	(46,718)	(28,997)	(17,721)	(135,177)	(79,933)	(55,244)
Interest and other income, net	1,009	39	970	1,534	528	1,006
Loss before income taxes	(45,709)	(28,958)	(16,751)	(133,643)	(79,405)	(54,238)
Provision for (benefit from) income taxes	—	(123)	123	—	87	(87)
Net loss	$ (45,709)	$ (28,835)	$ (16,874)	$ (133,643)	$ (79,492)	$ (54,151)

Collaboration Revenue

Our collaboration revenue for the three and nine months ended August 31, 2022 and 2021 is summarized as follows (in thousands):

	Three Months Ended August 31,			Nine Months Ended August 31,		
	2022	2021	Change	2022	2021	Change
Gilead	$ 7,182	$ 6,056	$ 1,126	$ 19,489	$ 12,522	$ 6,967
Sanofi	3,609	4,196	(587)	12,355	9,832	2,523
Total collaboration revenue	$ 10,791	$ 10,252	$ 539	$ 31,844	$ 22,354	$ 9,490

Our collaboration revenue increased by $0.5 million during the three months ended August 31, 2022 compared to the three months ended August 31, 2021. The increase of $1.1 million from our collaboration with Gilead was primarily due to increased effort resulting in a higher percentage of completion of performance obligations and an addition of $2.5 million to the transaction price from the achievement of a research milestone in August 2022. The decrease of $0.6 million from our collaboration with Sanofi was primarily due to the target substitutions in July 2022. The substitutions increased the overall forecasted costs and extended the research term of those targets, which offset the increases in revenue due to increased effort and resulted in less revenue recognized in the current period.

Our collaboration revenue increased by $9.5 million during the nine months ended August 31, 2022 compared to the nine months ended August 31, 2021 primarily due to increased effort resulting in a higher percentage of completion of performance obligations under our collaborations with Gilead and Sanofi in the current period. The increases were also due to additions to the transaction price from the achievement of research milestones totaling $10.0 million from our collaboration with Gilead and $2.0 million from our collaboration with Sanofi that resulted in higher revenue recognized in each period and impacted the cumulative catch up in revenue for activities satisfied in previous periods.

Research and Development Expenses

Our research and development expenses for the three and nine months ended August 31, 2022 and 2021 are summarized as follows (in thousands):

	Three Months Ended August 31,			Nine Months Ended August 31,		
	2022	2021	Change	2022	2021	Change
Compensation and related personnel costs	$ 17,290	$ 9,968	$ 7,322	$ 48,984	$ 26,832	$ 22,152
Stock-based compensation	4,229	2,212	2,017	11,766	5,450	6,316
Supplies and contract research	12,680	10,399	2,281	36,413	27,062	9,351
Preclinical activities	1,513	396	1,117	5,350	1,739	3,611
Contract manufacturing	3,014	3,147	(133)	10,738	6,514	4,224
Clinical costs	3,473	1,583	1,890	9,978	3,526	6,452
Facility and other costs	5,562	3,201	2,361	15,162	8,780	6,382
Total research and development expenses	$ 47,761	$ 30,906	$ 16,855	$ 138,391	$ 79,903	$ 58,488

Our research and development expenses increased by $16.9 million during the three months ended August 31, 2022 compared to the three months ended August 31, 2021. There was an increase in compensation and related personnel costs and in non-cash stock-based compensation expense of $7.3 million and $2.0 million, respectively, that were primarily attributable to higher headcount. The increase in non-cash stock-based compensation expense was also attributable to the issuance of restricted stock units (RSUs). There was also an increase in cost related to supplies and contract research and preclinical activities of $3.4 million as we continued to expand our preclinical development activities and drug discovery research, and an increase in clinical costs of $1.9 million primarily due to the ramping up of our clinical trial programs and ongoing patient enrollment.

Our research and development expenses increased by $58.5 million during the nine months ended August 31, 2022 compared to the nine months ended August 31, 2021. There was an increase in compensation and related personnel costs and in non-cash stock-based compensation expense of $22.2 million and $6.3 million, respectively, that were primarily attributable to higher headcount. The increase in non-cash stock-based compensation expense was also attributable to the issuance of RSUs. There was also an increase in cost related to supplies and contract research and preclinical activities of $13.0 million as we continued to expand our preclinical development activities and drug discovery research, and an increase in contract manufacturing and clinical costs of $10.7 million primarily due to the ramping up of our clinical trial programs and ongoing patient enrollment.

General and Administrative Expenses

Our general and administrative expenses increased by $1.4 million during the three months ended August 31, 2022 compared to the three months ended August 31, 2021. There was an increase of $0.3 million in compensation and related expenses and an increase of $0.7 million in non-cash stock-based compensation expense attributable to the issuance of RSUs and increased issuance of stock options. There was also an increase of $0.4 million in professional service and consulting expenses.

Our general and administrative expenses increased by $6.2 million during the nine months ended August 31, 2022 compared to the nine months ended August 31, 2021. There was an increase of $1.3 million in compensation related expenses and an increase of $2.6 million in non-cash stock-based compensation expense, both of which were primarily attributable to higher headcount. There was also an increase of $2.1 million in professional service expenses, including legal and accounting expenses related to infrastructure improvements.

Liquidity and Capital Resources

Sources of Liquidity

In July 2020, we closed our initial public offering (IPO) and issued 12,550,000 shares of our common stock (including the exercise by the underwriters of their option to purchase an additional 1,550,000 shares of common stock in August 2020) at a price to the public of $19.00 per share for net proceeds of $218.1 million, after deducting underwriting discounts and commissions of $16.7 million and expenses of $3.6 million.

In March 2021, we completed a follow-on offering and issued 5,175,000 shares of our common stock (including the exercise by the underwriters of their option to purchase an additional 675,000 shares of common stock) at a price to the public of $31.00 per share for net proceeds of $150.2 million, after deducting underwriting discounts and commissions of $9.6 million and expenses of $0.6 million.

In August 2021, we filed a shelf registration statement on Form S-3 on file with the SEC. This shelf registration statement, which includes a base prospectus, allows us at any time to offer and sell registered common stock, preferred stock, debt securities, warrants, subscriptions rights and units or any combination of such securities described in the prospectus in one or more offerings. In addition, we entered into an Equity Distribution Agreement with Piper Sandler & Co. (Piper Sandler) pursuant to which, from time to time, we may offer and sell through Piper Sandler up to $150.0 million of the common stock registered under the shelf registration statement pursuant to one or more "at the market" offerings. We are not required to sell any shares at any time during the term of the Equity Distribution Agreement. We agreed to pay Piper Sandler a commission of 3% of the gross sales price of any shares sold pursuant to the Equity Distribution Agreement. In June 2022, we issued and sold 2,000,000 shares of common stock under the Equity Distribution Agreement at a price of $10.0001 per share of common stock for net proceeds of approximately $19.3 million after deducting offering commissions and expenses paid by us (the June 2022 ATM Offering). As of August 31, 2022, we had $130.0 million of common stock remaining available for sale under the Equity Distribution Agreement.

In July 2022, we entered into separate securities purchase agreements with certain purchasers to issue and sell pre-funded warrants to purchase an aggregate of 6,814,920 shares of our common stock in registered direct offerings (RDOs) at a price of $13.939 per pre-funded warrant. Net proceeds from the RDOs were approximately $94.8 million, after deducting offering expenses of $0.2 million. The pre-funded warrants were immediately exercisable, have an exercise price of $0.001 and may be exercised at any time after the date of issuance. A holder of the pre-funded warrants may not exercise the warrant if the holder, together with its affiliates, would beneficially own more than 9.99% of the number of shares of our common stock outstanding immediately after giving effect to such exercise. A holder of the pre-funded warrants may increase or decrease this percentage not in excess of 19.99% by providing us at least 61 days' prior notice. As of August 31, 2022, all of the pre-funded warrants remained available for exercise.

Unless otherwise specified in a prospectus supplement accompanying the base prospectus, we intend to use the net proceeds from the sale of any securities offered pursuant to the shelf registration statement for general corporate purposes, which may include funding research, clinical and process development, increasing our working capital, reducing indebtedness, acquisitions or investments in businesses, products or technologies that are complementary to our own and capital expenditures. Pending such uses, we may invest the net proceeds in marketable securities that may include investment-grade interest-bearing securities, money market accounts, certificates of deposit, commercial paper and guaranteed obligations of the U.S. government.

Funding Requirements

As of August 31, 2022, our operations have primarily been funded through the net proceeds from equity offerings of $650.5 million and proceeds from collaborations of $310.0 million. We do not have any products approved for sale, and we have not generated any revenue from product sales. As of August 31, 2022, we had $413.6 million in cash, cash equivalents and marketable securities.

We expect that our existing cash, cash equivalents and marketable securities are sufficient to meet our cash requirements and continue operating activities, including the clinical trials of our drug candidates NX-2127, NX-1607, NX-5948 and DeTIL-0255 and the expansion of our intellectual property portfolio and infrastructure, for at least the next 12 months. We will need substantial additional funding to support our continuing operations and pursue our long-term business plan. We may seek to raise any necessary additional capital through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing and distribution arrangements. Because of the numerous risks and uncertainties associated with the development and commercialization of our drug candidates and the extent to which we may enter into additional collaborations with third parties to participate in their development and commercialization, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated pre-clinical studies and clinical trials.

In the long term, our ability to support our working capital and capital expenditure requirements will depend on many factors, including the following:

- the progress, costs and results of our ongoing Phase 1 clinical trials for our lead drug candidates NX-2127, NX-1607, NX-5948 and DeTIL-0255, and any future clinical development of such drug candidates;

- the scope, progress, costs and results of preclinical and clinical development for our other drug candidates and development programs;
- the number and development requirements of other drug candidates that we pursue;
- the scope of, and costs associated with, future advancements to our DELigase platform;
- the success of our collaborations with Sanofi, Gilead and any other collaborations we may establish;
- the costs, timing and outcome of regulatory review of our drug candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our drug candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our drug candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- our ability to establish additional collaboration arrangements with other biotechnology or pharmaceutical companies on favorable terms, if at all, for the development or commercialization of our drug candidates.

If adequate funds are not available at favorable terms, we may be required to reduce operating expenses, delay or reduce the scope of our product development and commercial expansion programs, obtain funds through arrangements with others that may require us to relinquish rights to certain of our technologies or products that we would otherwise seek to develop or commercialize ourselves, or cease operations. If we do raise additional capital through public or private equity or convertible debt offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

As of August 31, 2022, our material cash requirements include the following contractual and other obligations (in thousands):

	Payments due by period				
	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years	Total
Operating lease obligations	$ 6,487	$ 12,965	$ 5,380	$ 23,248	$ 48,080
Total contractual obligations	$ 6,487	$ 12,965	$ 5,380	$ 23,248	$ 48,080

In addition, we enter into agreements in the normal course of business with contract research organizations for clinical trials and with vendors for preclinical studies and other services and products for operating purposes, which are generally cancelable upon written notice. These payments are not included in the table above.

We did not have during the periods presented, and we do not currently have, any commitments or obligations, including contingent obligations, arising from arrangements with unconsolidated entities or persons that have or are reasonably likely to have a material current or future effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, cash requirements or capital resources.

Cash flows

Our cash flows for the nine months ended August 31, 2022 and 2021 are summarized as follows (in thousands):

	Nine Months Ended August 31,	
	2022	2021
Cash used in operating activities	$ (121,852)	$ (53,454)
Cash used in investing activities	(27,810)	(71,728)
Cash provided by financing activities	117,327	153,382
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (32,335)	$ 28,200

Operating activities

Net cash used in operating activities was $121.9 million for the nine months ended August 31, 2022 and consisted of a net loss of $133.6 million and an increase in net assets of $17.1 million, offset by non-cash adjustments of $28.9 million. The increase in net assets consisted of a decrease in deferred revenue of $22.3 million as we increased effort in our programs and recognized revenue, a decrease in operating lease liabilities of $3.7 million and an increase in prepaid expenses and other assets of $2.3 million primarily related to increased prepaid clinical and contract manufacturing costs and software license costs, offset by a decrease in accounts receivable of $6.0 million related to payments received under the Gilead Agreement, an increase in accrued expenses and other liabilities of $4.2 million primarily related to equipment purchases and the accrual of annual incentive compensation and an increase in accounts payable of $1.0 million. Non-cash adjustments primarily consisted of stock-based compensation expenses of $19.8 million, amortization of operating lease right-of-use assets of $4.0 million and depreciation and amortization expenses of $3.7 million.

Net cash used in operating activities was $53.5 million for the nine months ended August 31, 2021 and consisted of our net loss of $79.5 million, offset by a decrease in net assets of $9.4 million and non-cash adjustments of $16.7 million. The decrease in net assets consisted primarily of an increase in deferred revenue of $10.6 million, a decrease in income tax receivable of $3.6 million due to refunds received, an increase in accrued and other liabilities of $2.8 million, offset by an increase in prepaid expenses and other assets of $6.0 million primarily due to increased prepaid clinical costs and a decrease in operating lease liabilities of $2.4 million. Non-cash adjustments primarily consisted of stock-based compensation expenses of $11.0 million, amortization of operating lease right-of-use assets of $2.4 million and depreciation and amortization expenses of $2.0 million.

Investing activities

Net cash used in investing activities was $27.8 million for the nine months ended August 31, 2022 and consisted of the purchase of marketable securities of $212.5 million and the purchase of property and equipment of $9.7 million, offset by the maturity of marketable securities of $194.3 million.

Net cash used in investing activities was $71.7 million for the nine months ended August 31, 2021 and consisted of the purchase of marketable securities of $257.8 million and the purchase of property and equipment of $4.8 million, offset by the sale of marketable securities of $7.0 million and the maturity of marketable securities of $183.9 million.

Financing activities

Net cash provided by financing activities was $117.3 million for the nine months ended August 31, 2022 and consisted primarily of net proceeds from the issuance of pre-funded warrants in the RDOs of $94.9 million and from the issuance of common stock in the June 2022 ATM Offering of $19.4 million.

Net cash provided by financing activities was $153.4 million for the nine months ended August 31, 2021 and consisted primarily of proceeds from the issuance of common stock from a follow-on offering in March 2021.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

Our market risks, as of August 31, 2022, have not changed materially from those discussed in "Item 7A. Quantitative and Qualitative Disclosures About Market Risk" of our Annual Report on Form 10-K for the year ended November 30, 2021, filed with the SEC on January 28, 2022. As a "smaller reporting company" we are no longer required to provide the information required under this Item.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our President and Chief Executive Officer and our Chief Financial Officer, our principal executive officer and principal accounting and financial officer, respectively, have evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of August 31, 2022.

Disclosure controls and procedures are controls and other procedures that are designed to ensure that information required to be disclosed in our reports filed or submitted under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include controls and procedures designed to ensure that information required to be disclosed in our reports filed under the Exchange Act is accumulated and communicated to management, including our President and Chief Executive Officer and our Chief Financial Officer, to allow timely decisions regarding required disclosure. Based on the evaluation of our disclosure controls and procedures, our President and Chief Executive Officer and our Chief Financial Officer concluded that our disclosure controls and procedures were not effective as of August 31, 2022 due to the material weakness in our internal control over financial reporting described below.

In light of this fact, our management has performed additional analyses, reconciliations, and other post-closing procedures and has concluded that, notwithstanding the material weakness in our internal control over financial reporting, the condensed consolidated financial statements for the periods covered by and included in this Quarterly Report on Form 10-Q fairly present, in all material respects, our financial position, results of operations and cash flows as of and for the periods presented in conformity with U.S. GAAP.

Previously Reported Material Weakness in Internal Control over Financial Reporting

We have previously identified in our Annual Report on Form 10-K filed on January 28, 2022 the following control deficiencies that constitute material weaknesses in our internal control over financial reporting:

- We did not design and maintain effective controls over certain information technology (IT) general controls for IT systems that are relevant to the preparation of the financial statements. Specifically, we did not design and maintain: (a) user access controls to ensure appropriate segregation of duties and that adequately restrict user and privileged access to financial applications, programs, and data to appropriate personnel, and (b) program change management controls to ensure that IT program and data changes affecting financial IT applications and underlying accounting records are identified, tested, authorized and implemented appropriately. These IT deficiencies did not result in any misstatements to the financial statements; however, the deficiencies, when aggregated, could impact our ability to maintain effective segregation of duties, as well as the effectiveness of IT-dependent controls (such as automated controls that address the risk of material misstatement to one or more assertions, along with the IT controls and underlying data that support the effectiveness of system-generated data and reports) that could result in misstatements potentially impacting all financial statement accounts and disclosures that would result in a material misstatement to the annual or interim financial statements that would not be prevented or detected. Accordingly, management has determined that these deficiencies in the aggregate constitute a material weakness.
- We did not design and maintain effective segregation of duty controls over the review and approval of account reconciliations and manual journal entries. This material weakness did not result in any misstatements to the financial statements; however, the deficiency could result in a misstatement of substantially all of our account balances or disclosures that would result in a material misstatement to the annual or interim financial statements that would not be prevented or detected.

These material weaknesses could result in a misstatement of substantially all of our account balances or disclosures that would result in a material misstatement to the annual or interim financial statements that would not be prevented or detected. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis.

Remediation Plan

To address our material weaknesses, we have implemented and continue to implement new IT controls. We intend to continue to take steps to remediate the material weaknesses through formalizing documentation of IT policies and procedures and ensuring the ongoing operating effectiveness of the newly implemented IT controls to support effective IT dependent controls and our ability to maintain segregation of duties for our accounting staff in relation to account reconciliations and manual journal entries.

While we believe that these efforts will improve our internal control over financial reporting, the design and implementation of our remediation is ongoing and will require validation and testing of the design and operating effectiveness of our internal controls over a sustained period of financial reporting cycles. The actions that we are taking are subject to ongoing senior management review, as well as audit committee oversight. We will not be able to conclude whether the steps we are taking will fully remediate the material weaknesses in our internal control over financial reporting until we have completed our remediation efforts and subsequent evaluation of their effectiveness.

Changes in Internal Control Over Financial Reporting

As described under the Remediation Plan above, we continued formalizing documentation of our IT policies and procedures and implementing new controls during the three months ended August 31, 2022. Such remediation actions were changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the three months ended August 31, 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

From time to time, we may be involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, in the opinion of management, would have a material adverse effect on our business or condensed consolidated financial statements. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm and other factors.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. Before making your decision to invest in shares of our common stock, you should carefully consider the risks and uncertainties described below, together with all of the other information contained in this Quarterly Report on Form 10-Q, including our condensed consolidated financial statements and related notes and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations." We cannot assure you that any of the events discussed below will not occur. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of or that we deem immaterial may also become important factors that adversely affect our business. If any of the following risks occur, our business, financial condition, operating results, and future prospects could be materially and adversely affected. If that were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment.

Risk Factors Summary

Our business is subject to a number of risks and uncertainties, including those risks discussed at-length below. These risks include, among others, the following:

- We have incurred significant losses since our inception. We expect to incur losses over at least the next several years and may never achieve or maintain profitability.
- We have never generated revenue from product sales and may never be profitable.
- We will need substantial additional funding. If we are unable to raise capital when needed, we may be required to delay, limit, reduce or terminate our research or product development programs or future commercialization efforts.
- We are early in our development efforts. Our lead drug candidates, NX-2127, NX-1607, NX-5948 and DeTIL-0255 recently entered clinical development. If we are unable to advance our drug candidates through clinical development, develop, obtain regulatory approval for and commercialize our drug candidates or experience significant delays in doing so, our business may be materially harmed.
- Our limited operating history may make it difficult to evaluate the success of our business to date and to assess our future viability.
- If serious adverse events, undesirable side effects, or unexpected characteristics are identified during the development of any drug candidates we may develop, we may need to abandon or limit our further clinical development of those drug candidates.
- The results of preclinical studies and early-stage clinical trials may not be predictive of future results. Initial success in clinical trials may not be indicative of results obtained when these trials are completed or in later-stage trials.
- If we decide to seek Orphan Drug Designation or other designations from regulators for any of our current or future drug candidates, we may be unsuccessful or may be unable to maintain the benefits associated with these designations, including the potential for supplemental market exclusivity associated with an Orphan Drug Designation.
- If any of our drug candidates are not considered to be a new active substance or are deemed to fall within the "global marketing authorization" of an existing medicinal product or if pediatric studies are not adequately completed, this may result in lack of regulatory data protection or failure to obtain an extension to existing regulatory data protection.
- We face substantial competition in an environment of rapid technological change, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- We expect to depend on collaborations with third parties for the research, development and commercialization of certain of the drug candidates we may develop. If any such collaborations are not successful, we may not be able to capitalize on the market potential of those drug candidates.

- We rely on third-party contract manufacturing organizations (CMOs) for the manufacture of both drug substance and finished drug product for our drug candidates for preclinical and clinical testing and expect to continue to do so for any future clinical trials and commercialization. This reliance on third parties may increase the risk that we will not have sufficient quantities of our drug candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.
- If we are unable to obtain and maintain patent protection for our technology, our current drug candidates and any future drug candidates that we may develop, or if the scope of the patent protection obtained is not sufficiently broad, our competitors and other third parties could develop and commercialize technology and drug candidates similar or identical to ours, and our ability to successfully commercialize our technology and drug candidates may be impaired, and we may not be able to compete effectively in our market.
- Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on our business.
- Unfavorable global economic conditions could adversely affect our business, financial condition, stock price and results of operations.
- If we fail to attract and retain management and other key personnel, we may be unable to continue to successfully develop our current and any future drug candidates, commercialize our drug candidates or otherwise implement our business plan.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to incur losses over at least the next several years and may never achieve or maintain profitability.

Our net loss was $117.2 million for the fiscal year ended November 30, 2021, and $133.6 million for the nine months ended August 31, 2022. As of August 31, 2022, we had an accumulated deficit of $354.5 million. To date, we have not generated any revenue from product sales and have financed our operations primarily through our collaborations and sales of our equity interests. We are in the early stages of development of our drug candidates. Our lead drug candidates, NX-2127, NX-1607, NX-5948 and DeTIL-0255 recently entered clinical development. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We anticipate that our operating expenses and capital expenditure requirements will increase substantially if and as we:

- increase enrollment in our Phase 1 clinical trials of our drug candidates NX-2127, NX-1607, NX-5948 and DeTIL-0255;
- submit investigational new drug applications (INDs) and initiate clinical trials of our other drug candidates;
- enter advanced clinical development and scale up external manufacturing capabilities to supply clinical trials;
- expand the capabilities of our DELigase platform and apply our DELigase platform to advance additional drug candidates into preclinical and clinical development;
- conduct process development for manufacturing of our DeTIL cell therapy products;
- seek marketing approvals for any drug candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we may obtain marketing approval;
- expand, maintain and protect our intellectual property portfolio;
- hire additional clinical, regulatory, manufacturing, quality assurance and scientific personnel; and
- add operational, financial and management information systems and personnel to support our research, product development and future commercialization efforts and support our operations as a public company.

Our expenses could increase beyond our expectations if we are required by the FDA, the European Medicines Agency (EMA) or other regulatory authorities to perform trials in addition to those we currently expect, or if there are any delays in establishing appropriate manufacturing arrangements for or in completing our planned clinical trials or the development of any of our drug candidates.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we will incur or when, if ever, we will be able to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We have never generated revenue from product sales and may never be profitable.

We recently commenced clinical development of our drug candidates NX-2127, NX-1607, NX-5948 and DeTIL-0255. We expect that it will be many years, if ever, before we have a drug candidate ready for commercialization. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. To become and remain profitable, we must succeed in developing, obtaining marketing approval for and commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our drug candidates, discovering additional drug candidates, establishing and maintaining arrangements with third parties for the manufacture of clinical supplies of our drug candidates, obtaining marketing approval for our drug candidates and manufacturing, marketing, selling and obtaining reimbursement for any products for which we may obtain marketing approval.

If one or more of the drug candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved drug candidate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

We will need substantial additional funding. If we are unable to raise capital when needed, we may be required to delay, limit, reduce or terminate our research or product development programs or future commercialization efforts.

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we conduct our Phase 1 clinical trials of NX-2127, NX-1607, NX-5948 and DeTIL-0255, grow our pipeline of drug candidates, expand the breadth of our DELigase platform, continue research and development, and initiate additional clinical trials of and potentially seek marketing approval for our lead programs and other drug candidates. In addition, if we obtain marketing approval for any of our drug candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, reimbursement, and sales and distribution. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be required to delay, limit, reduce or terminate our research, product development programs or any future commercialization efforts or grant rights to develop and market drug candidates that we otherwise would prefer to develop and market ourselves.

We had cash, cash equivalents and marketable securities of $413.6 million as of August 31, 2022. We believe that our existing cash, cash equivalents and marketable securities, will be sufficient to fund our operating expenses and capital expenditure requirements through at least the next 12 months. However, our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect, and we may need to seek additional funds sooner than planned. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. Our future capital requirements will depend on many factors, including:

- the progress, costs and results of our Phase 1 clinical trials for NX-2127, NX-1607, NX-5948, DeTIL-0255 and any future clinical development of such drug candidates;
- the scope, progress, costs and results of preclinical and clinical development for our other drug candidates and development programs;
- the number and development requirements of other drug candidates that we pursue;
- the scope of, and costs associated with, future advancements to our DELigase platform;
- the scope of, and costs associated with, future preclinical development of our DeTIL cell therapy products;
- the success of our collaborations with Sanofi, Gilead and any other collaborations we may establish;
- the costs, timing and outcome of regulatory review of our drug candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our drug candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our drug candidates for which we receive marketing approval;

- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- our ability to establish additional collaboration arrangements with other biotechnology or pharmaceutical companies on favorable terms, if at all, for the development or commercialization of our drug candidates.

We will need to raise substantial additional capital to complete the development and commercialization of our drug candidates. In addition, our drug candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives. Adequate additional funds may not be available to us on acceptable terms, or at all.

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

Until such time, if ever, as we can generate substantial revenue from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. Although we may receive potential future milestone payments under our collaborations with Sanofi and Gilead, we do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making acquisitions or capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, technologies, future revenue streams, research programs or drug candidates or grant licenses on terms that may not be favorable to us.

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

We commenced operations in 2009, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, conducting discovery and research activities, filing patent applications, identifying potential drug candidates, undertaking preclinical studies, establishing arrangements with third parties for the manufacture of initial quantities of our drug candidates and conducting early stage clinical trials. Our lead drug candidates recently entered clinical development and their risk of failure is high. We have not yet demonstrated our ability to successfully: complete any clinical trials, including large-scale, pivotal clinical trials; obtain marketing approvals; manufacture a commercial-scale product or arrange for a third party to do so on our behalf; or conduct market access, sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as an early-stage business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Risks Related to the Discovery and Development of Our Drug Candidates

We are early in our development efforts. Our lead drug candidates, NX-2127, NX-1607, NX-5948 and DeTIL-0255, recently entered clinical development. If we are unable to advance our drug candidates through clinical development, develop, obtain regulatory approval for and commercialize our drug candidates or experience significant delays in doing so, our business may be materially harmed.

We are early in our development efforts. Our lead drug candidates, NX-2127, NX-1607, NX-5948 and DeTIL-0255, recently entered clinical development and their risk of failure is high. We have invested substantially all of our efforts and financial resources in building our DELigase platform, in the identification and preclinical development of our current drug candidates, and in the preparation for and initiation of Phase 1 clinical trials for our lead drug candidates. Our ability to generate revenue from product sales, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of one or more of our drug candidates. The success of our drug candidates will depend on several factors, including the following:

- sufficiency of our financial and other resources;
- successful completion of preclinical studies;
- successful submission of INDs or Clinical Trial Applications and initiation of clinical trials;
- successful patient enrollment in, and completion of, clinical trials;
- receipt and related terms of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our drug candidates;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our drug candidates;
- achieving desirable therapeutic properties for our drug candidates' intended indications;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- obtaining and maintaining third-party coverage and adequate reimbursement;
- establishing a continued acceptable safety profile of the products and maintaining such a profile following approval; and
- effectively competing with other therapies.

If we do not successfully achieve 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 drug candidates, which could materially harm our business. Moreover, if we do not receive regulatory approvals, we may not be able to continue our operations.

One of our approaches to the discovery and development of drug candidates based on our targeted protein degradation platform is unproven, which makes it difficult to predict the time, cost of development and likelihood of successfully developing any products.

Treating diseases using targeted protein degradation is a new treatment modality. Our future success depends on the successful development of this novel therapeutic approach. Very few small molecule drug candidates designed to control cellular protein levels, such as our BTK degraders, have been tested in humans, none has been approved in the United States or Europe, and the data underlying the feasibility of developing these therapeutic products is both preliminary and limited. Discovery and development of targeted protein degraders that harness ligases to degrade protein targets have been impeded largely by the complexities and limited understanding of the functions, biochemistry and structural biology of E3 ligases as well as by challenges of engineering compounds that promote protein-protein interactions.

We believe that our targeted protein degrader drug candidates may offer an improved therapeutic approach by removing the disease-causing proteins instead of simply inhibiting their activities. However, the scientific research that forms the basis of our efforts to develop our targeted protein degrader drug candidates is ongoing and the scientific evidence to support the feasibility of developing targeted protein degrader-based therapeutic treatments is both preliminary and limited. Further, certain patients have shown inherent primary resistance to approved BTK inhibitors and other patients have developed acquired secondary resistance to these inhibitors. Based on preclinical animal models and observations in human primary blood cells, we believe that both NX-2127 and NX-5948 are able to degrade BTK with mutations that confer resistance to currently marketed BTK inhibitors, and we believe that preliminary data from our ongoing Phase 1 trial of NX-2127 may provide evidence of such degradation in humans. However, any inherent primary or acquired secondary resistance to our BTK degraders in patients would prevent or diminish their clinical benefit.

We recently initiated clinical development of NX-2127 and NX-5948 and currently we have limited safety data of NX-2127 and NX-5948 in humans. Although some of our drug candidates have produced observable results in animal studies, these drug candidates may not demonstrate the same chemical and pharmacological properties in humans, and may interact with human biological systems in unforeseen, ineffective or harmful ways. As such, there may be adverse effects from treatment with any of our current or future drug candidates that we cannot predict at this time.

Additionally, the regulatory approval process for novel drug candidates such as ours can be more expensive and take longer than for other, better-known or extensively-studied drug candidates. Although other companies are also developing therapeutics based on targeted protein degradation, no regulatory authority has granted approval for any such therapeutic. As a result of these factors, it is more difficult for us to predict the time and cost of targeted protein degrader drug candidate development, and we cannot predict whether targeted protein degradation will result in the development and marketing approval of any products. Any development problems we experience in the future related to any of our targeted protein degrader research programs may cause significant delays or unanticipated costs or may prevent the development of a commercially viable product. Advancing our targeted protein degrader products creates significant challenges for us, including:

- educating medical personnel regarding the potential efficacy and safety benefits, as well as the challenges, of incorporating our drug candidates, if approved, into treatment regimens; and
- establishing the sales and marketing capabilities to gain market acceptance, if approved.

Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate, or from commercializing any targeted protein degrader drug candidates we may develop on a timely or profitable basis, if at all.

Drug development is a lengthy and expensive process, with an uncertain outcome. We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug candidates.

Our lead drug candidates recently entered clinical development and their risk of failure is high. We are unable to predict when or if any of our drug candidates will prove effective or safe in humans or will receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any drug candidate, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. Before we can commence clinical trials for a drug candidate, we must complete extensive preclinical testing and studies that support our planned INDs in the United States or similar applications in other jurisdictions. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or similar regulatory authorities outside the United States will accept our proposed clinical programs or if the outcome of our preclinical testing and studies ultimately will support the further development of our programs.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to the outcome. A failure of one or more clinical trials can occur at any stage of testing. Clinical trials may produce negative or inconclusive results, and we or any future collaborators may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. We will be required to demonstrate with substantial evidence through adequate and well-controlled clinical trials that our drug candidates are safe and effective for use in treating specific conditions in order to obtain marketing approvals for their commercial sale. Success in preclinical studies and early-stage clinical trials does not mean that any future larger registration clinical trials will be successful because drug candidates in later-stage clinical trials may fail to demonstrate safety and efficacy to the satisfaction of the FDA and non-U.S. regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials. Drug candidates that have shown promising results in preclinical studies and early-stage clinical trials may still suffer significant setbacks in subsequent registration clinical trials. Additionally, the outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later-stage clinical trials.

We may experience numerous unforeseen events during, or as a result of, clinical trials, that could delay or prevent our ability to receive marketing approval or commercialize our drug candidates, including:

- we may experience delays in reaching, or may fail to reach, a consensus with regulators on trial design;
- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate, including as a result of delays in the testing, validation, manufacturing and delivery of drug candidates to the clinical sites by us or by third parties with whom we have contracted to perform certain of those functions;
- we may experience delays in reaching, or may fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- regulators or institutional review boards (IRBs) may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;

- we may face delays under human tissue act legislation and restrictions across various jurisdictions;
- we may experience difficulty in designing clinical trials and in selecting endpoints for diseases that have not been well-studied and for which the natural history and course of the disease is poorly understood;
- the selection of certain clinical endpoints may require prolonged periods of clinical observation or analysis of the resulting data;
- the number of patients required for clinical trials of our drug candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our drug candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs to suspend or terminate the trials;
- we may have to suspend or terminate clinical trials of our drug candidates for various reasons, including a partial or full clinical hold based on a finding that our drug candidates have undesirable side effects or other unexpected characteristics, or that the participants are being exposed to unacceptable health risks;
- 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;
- regulators or IRBs may require that we or our investigators suspend or terminate clinical trials for various reasons, including noncompliance with regulatory requirements;
- clinical trials of our drug candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the cost of clinical trials of our drug candidates may be greater than we anticipate;
- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate;
- regulators may revise the requirements for approving our drug candidates, or such requirements may not be as we anticipate;
- any future collaborators that conduct clinical trials may face any of the above issues and may also conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us; and
- disruptions caused by the COVID-19 pandemic, including supply chain disruptions, may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same drug candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain marketing approval to market our drug candidates.

If we are required to conduct additional clinical trials or other testing of our drug candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our drug candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our drug candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements or changes in the way the product is administered; or
- have the product removed from the market after obtaining marketing approval.

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

Further, cancer therapies sometimes are characterized as first-line, second-line, or third-line, and the FDA often approves new therapies initially only for third-line or later use, meaning for use after two or more other treatments have failed. When cancer is detected early enough, first-line therapy, usually chemotherapy, hormone therapy, immunotherapy, radiation therapy, surgery, targeted 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. Our current and planned clinical trials for our drug candidates NX-2127, NX-1607, NX-5948 and DeTIL-0255 are and will be with patients who have received one or more prior treatments. Subsequently, for those products that prove to be sufficiently beneficial, if any, we may seek approval potentially as a first-line therapy, but any drug candidates we develop, even if approved, may not be approved for first-line therapy, and, prior to any such approvals, we may have to conduct additional clinical trials.

If serious adverse events, undesirable side effects, or unexpected characteristics are identified during the development of any drug candidates we may develop, we may need to abandon or limit our further clinical development of those drug candidates.

We have recently begun to evaluate our lead drug candidates in human clinical trials, and there have been very few clinical trials to date involving small molecule drug candidates designed to control cellular protein levels through targeted protein degradation. It is impossible to predict when or if any drug candidates we may develop will prove safe in humans. There is a limited safety data set for the effects of NX-2127, NX-1607, NX-5948 and DeTIL-0255 in animals and we only recently have begun to test the safety of our drug candidates in humans. There can be no assurance that our current drug candidates or any future drug candidate will not cause undesirable side effects. Unforeseen side effects from our drug candidates could arise at any time during preclinical or clinical development.

A potential risk in any protein modulation product is that healthy proteins or proteins not targeted for modulation will be modulated or that the modulation of the targeted protein in itself could cause adverse events, undesirable side effects or unexpected characteristics. It is possible that healthy proteins or proteins not targeted for modulation could be modulated by our drug candidates in any of our current or future clinical studies. There also is the potential risk of delayed adverse events following treatment with our drug candidates.

If any drug candidates we develop are associated with serious adverse events, or undesirable side effects, or have characteristics that are unexpected, including in preclinical studies, we may need to abandon their development or limit development to certain uses or subpopulations in which the adverse events, undesirable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk-benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations, and prospects. For example, increased bleeding risk and cardiac arrhythmia such as atrial fibrillation have been reported side effects of approved BTK inhibitors. Furthermore, NX-1607 could activate the immune response to unsafe levels and may have the potential to induce hypercytokinemia, or cytokine storm, which is the overstimulation of immune cells and subsequent overproduction of their activating compounds. Many drug candidates that initially showed promise in early-stage testing for treating cancer or other diseases later have been found to cause side effects that prevented further clinical development of the drug candidates or limited their competitiveness in the market.

The results of preclinical studies and early-stage clinical trials may not be predictive of future results. Initial success in clinical trials may not be indicative of results obtained when these trials are completed or in later-stage trials.

The results of preclinical studies may not be predictive of the results of clinical trials, and the results of any early-stage clinical trials we commence may not be predictive of the results of the later-stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. In particular, the small number of patients in our planned early clinical trials may make the results of these trials less predictive of the outcome of later clinical trials. For example, even if successful, the results of our initial clinical trials for NX-2127, NX-1607, NX-5948 and DeTIL-0255 may not be predictive of the results of further clinical trials of these drug candidates or any of our other drug candidates. Moreover, preclinical and clinical data often are susceptible to varying interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in preclinical studies and clinical trials nonetheless have failed to obtain marketing approval of their products. Our future clinical trials may not ultimately be successful or support further clinical development of any of our drug candidates. There is a high failure rate for drug candidates proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving encouraging results in earlier studies. Any such setbacks in our clinical development could materially harm our business, results of operations, financial condition and prospects.

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

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

If we experience delays or difficulties in enrolling patients in clinical trials, our receipt of necessary marketing approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our drug candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. In particular, we are currently conducting Phase 1 clinical trials for each of our four lead drug candidates: NX-2127, NX-1607, NX-5948 and DeTIL-0255. We cannot predict how difficult it will be to enroll patients for these trials. Therefore, our ability to identify and enroll eligible patients for our NX-2127, NX-1607, NX-5948 and DeTIL-0255 clinical trials may be limited or may result in slower enrollment than we anticipate. In addition, some of our competitors have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates, and patients who otherwise would be eligible for our planned clinical trials instead may enroll in clinical trials of our competitors' drug candidates. Moreover, the size of the relevant patient populations for the diseases that our lead drug candidates target is small, and as more companies begin to focus attention and resources on drug candidates to treat the same indications as our drug candidates, we may experience delays or be unable to successfully recruit and enroll a sufficient number of eligible patients in our clinical trials. Patient enrollment is affected by other factors including:

- the severity of the disease under investigation;
- the size of the patient population and process for identifying patients;
- the availability and efficacy of approved medications for the disease under investigation;
- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the drug candidates under study;
- the efforts to facilitate timely enrollment in clinical trials;
- physicians' attitudes and practices with respect to clinical trial enrollment;
- the burden on patients due to inconvenient procedures;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients; and
- the impact of the current COVID-19 pandemic, which may affect the conduct of a clinical trial, including by slowing potential enrollment or reducing the number of eligible patients for clinical trials.

Our inability to enroll a sufficient number of patients for our current or planned clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our current or planned clinical trials may result in increased development costs for our drug candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

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

Because we have limited financial and managerial resources, we focus on research programs and drug candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and drug candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug 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 drug candidate.

The manufacture of drugs is complex and we and our third-party manufacturers are early in our manufacturing efforts.

We have established manufacturing relationships with a limited number of suppliers to manufacture raw materials and the drug substance of any drug candidate for which we now are pursuing, or may in the future pursue, preclinical or clinical development. Our systems for complying with current good manufacturing practices (cGMPs), manufacturing process development with our third-party manufacturers and scale-up is at an early stage. The actual cost to manufacture and process our drug candidates could be greater than we expect and could materially and adversely affect the commercial viability of our drug candidates. Our third-party manufacturers may encounter difficulties in production, including 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 any of our third-party manufacturers encounter such difficulties, our ability to provide supply of our current or future drug candidates for clinical trials, our ability to obtain marketing approval, or our ability to provide supply of our drug candidates for patients, if approved, could be delayed or stopped.

We have limited experience with the development and manufacturing of adoptive cellular therapeutics, which is a relatively new and expanding category of therapeutics with unique development, manufacturing and regulatory risks.

We are exploring the use of T cell-enhancing compounds to improve the current industry-standard methods and technology for adoptive cellular therapies (ACTs) in both hematologic cancers and solid tumors. ACTs represent a class of immunotherapy in which T cells are isolated directly from patient tumors, as with TIL, or from patient blood with subsequent genetic modification to recognize specific antigens present on cancer cells, as with CAR-T therapies. These tumor-reactive T cells are then expanded and infused back into the patient. These cell therapy technologies are a relatively new and expanding category of therapeutics, with which we have limited experience. We may observe undesirable characteristics such as cytokine storm, immunogenicity, infection or other adverse events. Additionally, because TIL and CAR-T therapies are manufactured on a patient-by-patient basis, they require extensive research and development and involve complex and costly manufacturing. Moreover, we anticipate that we will have to rely on third-party manufacturers to manufacture our ACT products for pre-clinical studies and clinical trials and if they fail to commence or complete, or experience delays in, manufacturing ACT products, our pre-clinical studies and clinical trials will be delayed. The FDA and other regulatory bodies also have limited experience with ACTs, which may result in regulatory delays. The regulatory pathway is complex and may take more time and be more expensive to pursue than the regulatory pathway for other established drug candidates. Moreover, the FDA regulatory pathway for our DeTIL and CAR-T programs is not clear and may require us to file a Biologics License Application or an application for a Combination Product and will be subject to further discussion with regulators. Because this is a relatively new and expanding area, there are many uncertainties related to the appropriate regulatory pathway, development, manufacturing, marketing, reimbursement, and the commercial potential for these drug candidates, and we may never be successful in developing these therapeutics.

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

A key element of our strategy is to apply our DELigase platform to address a broad array of targets and new therapeutic areas. The therapeutic discovery activities we are conducting may not be successful in identifying drug candidates that are useful in treating hematologic cancers, immune-mediated diseases or any other diseases. Our research programs initially may show promise in identifying potential drug candidates, yet fail to yield drug candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential drug candidates;
- potential drug candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval or achieve market acceptance; or
- potential drug candidates may not be effective in treating their targeted diseases.

Research programs to identify new drug candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential drug candidate that ultimately proves to be unsuccessful. If we are unable to identify suitable drug candidates for preclinical and clinical development, we will not be able to obtain revenues from the sale of products in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

We may not be successful in our efforts to expand the breadth of our DELigase platform.

A key element of our strategy is to expand the capabilities of our DELigase platform and leverage our platform to discover, develop and potentially commercialize additional drug candidates beyond our current portfolio to target diseases in a wide range of organ systems and tissues and treat various disease states. These enhancements require substantial technical, financial and human resources, and may not result in the discovery or development of additional drug candidates or therapies. We may pursue what we believe is a promising opportunity to leverage our platform only to discover that certain of our risk or resource allocation decisions were incorrect or insufficient, or that individual products or our science in general has technology or biology risks that were previously unknown or underappreciated. Our strategy of pursuing the value of our DELigase platform over a long-time horizon and across a broad array of human diseases may not be effective. In the event material decisions in any of these areas turn out to be incorrect or sub-optimal, we may experience a material adverse impact on our business and ability to fund our operations and we may never realize what we believe is the potential of our DELigase platform.

We face substantial competition in an environment of rapid technological change, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. Moreover, the biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face and will continue to face competition from third parties that use protein modulation, antibody therapy, ACT, inhibitory nucleic acid, gene editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities, such as small molecule inhibitors. The competition is likely to come from multiple sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, government agencies and other public and private research institutions that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing and commercialization.

We are aware of several biotechnology companies focused on developing small molecules that degrade target proteins including but not limited to Arvinas, Inc., BioTheryX, Inc., C4 Therapeutics, Inc., Cullgen Inc., Foghorn Therapeutics Inc., Kymera Therapeutics, Inc. and Monte Rosa Therapeutics, all of which currently are in preclinical or clinical development. In addition, several large pharmaceutical companies have disclosed preclinical investments in this field, including Amgen Inc., AstraZeneca plc, Bayer AG, Bristol-Myers Squibb Company, Genentech, Inc., GlaxoSmithKline plc and Novartis International AG. Furthermore, we are aware of several biotech companies focused on developing tumor infiltrating lymphocyte (TIL) therapies for the treatment of cancer, including Instil Bio, Inc., Iovance Biotherapeutics, Inc., PACT Pharma, Inc. and Lyell Immunopharma, Inc.

Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies also may prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in preventing us from obtaining the orphan designation in the European Union (EU) and/or in the United Kingdom (UK) and our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. There are generic products currently on the market for certain of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our drug candidates are approved, we expect that they will be priced at a significant premium over competitive generic products.

If we do not achieve our projected development goals in the time frames 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 and may be associated with payments from third-party collaborators such as Sanofi or Gilead. 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, our revenue may be lower than expected, the commercialization of our products may be delayed or never achieved and, as a result, our stock price may decline.

Our estimated market opportunities for our drug candidates are subject to numerous uncertainties and may prove to be inaccurate. If we have overestimated the size of our market opportunities, our future growth may be limited.

Our estimated addressable markets and market opportunities for our drug candidates are based on a variety of inputs, including data published by third parties, our own market insights and internal market intelligence, and internally generated data and assumptions. We have not independently verified any third-party information and cannot be assured of its accuracy or completeness. Market opportunity estimates, whether obtained or derived from third-party sources or developed internally, are subject to significant uncertainty and are based on assumptions and estimates that may prove not to be accurate. Although we believe our market opportunity estimates are reasonable, such information is inherently imprecise. In addition, our assumptions and estimates of market opportunities are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including but not limited to those described in this report. If this third-party or internally generated data prove to be inaccurate or if we make errors in our assumptions based on that data, our actual market may be more limited than we estimate it to be. In addition, these inaccuracies or errors may cause us to misallocate capital and other critical business resources, which could harm our business.

Risks Related to Dependence on Third Parties

We expect to depend on collaborations with third parties for the research, development, and commercialization of certain of the drug candidates we may develop. If any such collaborations are not successful, we may not be able to capitalize on the market potential of those drug candidates.

We have sought third-party collaborators for the research, development, and commercialization of some of our targeted protein degrader programs. For example, in June 2019 we entered into a collaboration with Gilead and in December 2019 we entered into a collaboration with Sanofi, which was subsequently expanded and amended in January 2021. Both collaborations require us to conduct certain research activities. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, biotechnology companies and universities. These and any future arrangements with third parties limit our control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of any drug candidates we may seek to develop with them. 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. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs or any drug candidates we may develop, including our collaborations with Sanofi and Gilead, pose risks to us, including:

- Collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations with us.
- Collaborators may not pursue development and commercialization of any drug candidates we may develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition or business combination that diverts resources or creates competing priorities.
- Sanofi and Gilead have broad option rights to select up to five targets each for exclusive targeted protein degrader development, so long as not excluded by us under the terms of each collaboration, and may select targets we are considering but have not taken sufficient action to exclude under each collaboration.
- Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a drug candidate, repeat or conduct new clinical trials, or require a new formulation of a drug candidate for clinical testing.
- Collaborators could develop independently, or develop with third parties, products that compete directly or indirectly with our products or drug 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 obtain, maintain, enforce or defend our intellectual property or proprietary rights or may use our proprietary information in such a way that could jeopardize or invalidate our proprietary information or expose us to potential litigation. For example, Sanofi and Gilead have the first right to enforce or defend certain intellectual property rights under the applicable collaboration arrangement with respect to particular licensed programs, and although we may have the right to assume the enforcement and defense of such intellectual property rights if the collaborator does not, our ability to do so may be compromised by their actions.
- Disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or drug candidates or that result in costly litigation or arbitration that diverts management attention and resources.
- We may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control. For example, Sanofi may terminate its agreement with us if we undergo a change of control.
- Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable drug candidates. For example, each of Sanofi and Gilead can terminate its agreement with us in its entirety or with respect to a specific target for convenience upon written notice or in connection with a material breach of the agreement by us that remains uncured for a specified period of time.
- Collaboration agreements may not lead to development or commercialization of drug candidates in the most efficient manner, or at all. For instance, if a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated.

If our collaborations do not result in the successful development and commercialization of products, or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of drug candidates could be delayed, and we may need additional resources to develop drug candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, marketing approval, and commercialization described in this report apply to the activities of our collaborators.

We may in the future decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of any drug candidates we may develop. These relationships may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute the ownership interest of our existing stockholders, or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement will depend upon, among other things, our assessment of the proposed collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of several factors. If we license rights to any drug candidates we or our collaborators may develop, 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 may seek to establish additional collaborations. If we are not able to establish collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.

We plan to continue to selectively pursue collaborations with leading biopharmaceutical companies with development and commercial expertise and capabilities. We face significant competition in attracting appropriate collaborators to advance the development of any drug candidates for which we may seek a collaboration. Whether we reach a definitive agreement for a collaboration will depend upon, among other things, our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of preclinical studies and clinical trials, the likelihood of approval by the FDA or other regulatory authorities, the potential market for the subject drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing products, 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), the terms of any existing collaboration agreements, and industry and market conditions generally. The collaborator also may have the opportunity to collaborate on other drug candidates or technologies for similar indications and will have to evaluate whether such a collaboration could be more attractive than one with us.

Collaborations are complex and time-consuming to negotiate, document and execute. In addition, consolidation among large pharmaceutical companies has reduced the number of potential future collaborators, and we may not be able to locate a suitable collaborator. Any collaboration we enter into may limit our ability to enter into future agreements on particular terms or covering similar target indications with other potential collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the drug candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we may not be able to further develop our drug candidates or bring them to market and generate revenue from product sales, which could have an adverse effect on our business, financial condition, results of operations and prospects.

We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for completing such trials.

We rely on third-party contract research organizations (CROs) to conduct our Phase 1 clinical trial programs for NX-2127, NX-1607, NX-5948 and DeTIL-0255 and we will rely on third-party CROs to conduct any clinical trials for other drug candidates. Agreements with these CROs might terminate for a variety of reasons, including for such CRO's failure to perform. Entry into alternative arrangements, if necessary, could significantly delay our product development activities.

Our reliance on these CROs for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols in the applicable IND. Moreover, the FDA requires compliance with standards, commonly referred to as GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected.

If these CROs do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our drug candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our drug candidates.

We rely on third-party contract manufacturing organizations for the manufacture of both drug substance and finished drug product for our drug candidates for preclinical and clinical testing and expect to continue to do so for any future clinical trials and commercialization. This reliance on third parties may increase the risk that we will not have sufficient quantities of our drug candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely on and expect to continue to rely on third-party CMOs for both drug substance and finished drug product, and ACT product. This reliance on CMOs, particularly where one CMO is the sole source of the drug substance or finished drug product, or ACT product, may increase the risk that we will not have sufficient quantities of our drug candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We may be unable to establish agreements with CMOs or to do so on acceptable terms. Even if we are able to establish agreements with CMOs, reliance on them entails additional risks, including:

- reliance on the CMO for regulatory, compliance and quality assurance;
- the possible breach of the manufacturing agreement by the CMO;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the CMO at a time that is costly or inconvenient for us.

We have only limited technology transfer agreements in place with respect to our drug candidates, and these arrangements do not extend to commercial supply. We acquire many key materials on a purchase order basis. As a result, we do not have long-term committed arrangements with respect to our drug candidates and other materials. If we receive marketing approval for any of our drug candidates, we will need to establish an agreement for commercial manufacture with a third party.

The CMOs we retain may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our CMOs, to comply with applicable regulations could result in sanctions or other adverse regulatory actions, including untitled or warning letters, clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, failure to approve pending applications, license revocation, seizures or recalls of drug candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

The facilities used by our contract manufacturers to manufacture our drug candidates must be approved by the FDA or the EMA or other national or international regulatory agencies pursuant to inspections that will be conducted after we submit our NDA to the FDA or our marketing authorization application (MAA) to the EMA or other regulatory authority. We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with cGMP regulations for manufacturing both active drug substances and finished drug products. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, the EMA or comparable foreign regulatory bodies, they will not be able to secure and/or maintain marketing approval for their manufacturing facilities. In addition, we do not have complete control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, the EMA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our drug candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our drug candidates, if approved.

Our drug candidates and any products that we may develop may compete with other drug candidates and products for access to suitable manufacturing facilities. As a result, we may not obtain access to these facilities on a priority basis or at all. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval or could result in withdrawal of marketing approval. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. If our current CMOs cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our drug candidates, we may incur added costs and delays in identifying and qualifying any such replacement manufacturer or may not be able to reach agreement with any alternative manufacturer.

Our current and anticipated future dependence upon others for the manufacture of our drug candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

Some of our suppliers may experience disruption to their respective supply chain due to the effects of the COVID-19 pandemic, which could delay, prevent or impair our development or commercialization efforts.

We obtain certain chemical or biological intermediates in the synthesis of our drug candidates and NHPs for toxicology testing in countries affected by the COVID-19 pandemic. If we are unable to obtain these chemical or biological intermediates or NHPs in sufficient quantity and in a timely manner due to disruptions in the global supply chain caused by the COVID-19 pandemic, the development, testing and clinical trials of that drug candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

Our CMOs may be unable to successfully scale-up manufacturing of our drug candidates in sufficient quality and quantity, which would delay or prevent us from developing our drug candidates and commercializing approved products, if any.

In order to conduct clinical trials of our drug candidates, we will need to manufacture our drug candidates in large quantities. Quality issues may arise during scale-up activities. Our reliance on a limited number of CMOs, the complexity of drug manufacturing and the difficulty of scaling up a manufacturing process could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our drug candidates, cause us to incur higher costs and prevent us from commercializing our drug candidates successfully. Furthermore, if our CMOs fail to deliver the required commercial quality and quantities of materials on a timely basis and at commercially reasonable prices, and we are unable to secure one or more replacement CMOs capable of production in a timely manner at a substantially equivalent cost, then testing and clinical trials of that drug candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

Risks Related to the Commercialization of Our Drug Candidates

Even if any of our drug candidates receive marketing approval, a drug candidate may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our drug candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, ibrutinib is a well-established current treatment for CLL and other B-cell malignancies, and doctors may continue to rely on this and other treatments. If our drug candidates do not achieve an adequate level of acceptance, we may not generate significant revenue from product sales and we may not become profitable. The degree of market acceptance of our drug candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- the prevalence and severity of any side effects, in particular compared to alternative treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing, sales and distribution support;
- the availability of third-party payor coverage and adequate reimbursement;
- the ability to secure a positive health technology appraisal (HTA) recommendation for the product to be prescribed and reimbursed under the national health system;
- the timing of any marketing approval in relation to other product approvals; and
- any restrictions on the use of our products together with other medications.

If we are unable to establish sales and marketing capabilities, we may not be successful in commercializing our drug candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of biopharmaceutical products. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish sales, marketing and distribution capabilities, either by ourselves or through collaboration or other arrangements with third parties.

We currently expect that we may build our own focused, specialized sales and marketing organization to support the commercialization in the United States of drug candidates for which we receive marketing approval and that can be commercialized with such capabilities. There are risks involved with establishing our own sales and marketing capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a drug candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have incurred these commercialization expenses prematurely or unnecessarily. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs, and other support personnel;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales and marketing capabilities or enter into arrangements with third parties to perform these services, our revenue from product sales and our profitability, if any, are likely to be lower than if we ourselves were to market and sell any products that we develop. In addition, we may not be successful in entering into arrangements with third parties to market and sell our drug candidates or may be unable to do so on terms that are acceptable to us. Any of these third parties may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our drug candidates.

Even if we are able to commercialize any drug candidates, the products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. 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. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our drug candidate to other available therapies. 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 drug 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, and negatively impact the revenues, if any, we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval.

Our ability to commercialize any drug candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government healthcare programs, private health insurers, national health technology assessment authorities in Europe and other organizations, and if reimbursement and coverage is available, the level of reimbursement and coverage. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A key focus in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, government authorities and 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. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any drug candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any drug 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 similar regulatory authorities outside of the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, also may not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, may take into account comparative cost-effectiveness, in particular in European jurisdictions, and may be incorporated into existing 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. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate 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.

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

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

- decreased demand for any drug candidates or products that we may develop;
- termination of clinical trials;
- withdrawal of marketing approval, recall, restriction on the approval or a “black box” warning or contraindication for an approved drug;
- withdrawal of clinical trial participants;

- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- injury to our reputation and significant negative media attention;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our product liability insurance coverage as we initiate our clinical trials, as we expand our clinical trials and if we commence commercialization of our drug candidates. Insurance coverage is increasingly expensive. We may not be able to maintain or increase our insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology, our current drug candidates and any future drug candidates that we may develop, or if the scope of the patent protection obtained is not sufficiently broad, our competitors and other third parties could develop and commercialize technology and drug candidates similar or identical to ours, and our ability to successfully commercialize our technology and drug candidates may be impaired, and we may not be able to compete effectively in our market.

Our commercial success depends, in large part, on our ability to obtain and maintain patent and other intellectual property and proprietary protection in the United States and other countries with respect to our drug candidates and proprietary technology. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and drug candidates. If we are unable to obtain or maintain patent protection with respect to our proprietary drug candidates and technology or do not otherwise adequately protect our intellectual property, competitors and other third parties may be able to use our drug candidates and technologies and erode or negate any competitive advantage that we may have, which could have a material adverse effect on our business. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors and other third parties to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. Moreover, the patent applications we own, co-own or license may fail to result in issued patents that cover our current and future drug candidates in the United States or in other foreign countries. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, a patent issues from such applications, and then only to the extent the issued claims cover the technology. If the patent applications we hold with respect to our development programs and drug candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our current and future drug candidates, it could have a material adverse effect on our ability to commercialize our drug candidates and our business.

To protect our proprietary positions, we file patent applications in the United States and other countries related to our novel technologies and drug candidates that are important to our business. The patent application and prosecution process is expensive, complex and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications in all potential jurisdictions 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 be able to obtain or maintain patent applications and patents due to the subject matter claimed in such patent applications and patents being in the public domain. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, such as with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If any current or future licensors or licensees are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised and we might not be able to prevent third parties from making, using and selling competing products. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Moreover, our competitors and other third parties may independently develop equivalent knowledge, methods and know-how. Any of these outcomes could impair our ability to prevent competition from third parties.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the protections offered by laws of different countries vary and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds and technologies commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights, whether owned or in-licensed, are highly uncertain. Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the U.S. federal courts, and the U.S. Patent and Trademark Office (USPTO), the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain patents or to enforce any patents that we might obtain in the future.

We may not be aware of all third-party intellectual property rights potentially relating to our current and future drug candidates. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions typically are not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we or our licensors were the first inventors to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications, whether owned or in-licensed, may not result in patents being issued that protect our technology or drug candidates, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. 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. Moreover, we may be subject to a third-party preissuance submission of prior art to the USPTO challenging the validity of one or more claims of our owned or licensed patents. Such submissions may also be made prior to a patent's issuance, precluding the granting of a patent based on one of our owned or licensed pending patent applications. We may become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or other post-grant proceedings, in the United States or elsewhere, challenging our or our licensors' 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, allow third parties to commercialize our technology or drug candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights, which could significantly harm our business and results of operations. Moreover, we, or one of our licensors, may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of patentability. Such challenges may result in loss of patent rights, exclusivity, freedom to operate, or in patent claims being narrowed, invalidated, or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drug candidates, or limit the duration of the patent protection of our technology and drug candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, any threat to the breadth or strength of protection provided by our patents and patent applications could dissuade companies from collaborating with us to license, develop or commercialize current or future drug candidates.

Even if our patent applications issue as patents and are unchallenged, they may not issue in a form that will provide us with any meaningful protection against competing products or processes sufficient to achieve our business objectives, prevent competitors and other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors and other third parties may be able to design around or circumvent our patents, should they issue, by developing similar or alternative technologies or products in a non-infringing manner. Our competitors and other third parties may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid and/or unenforceable. If the patent protection provided by the patents and patent applications we own or license is not sufficiently broad to impede such competition, our ability to successfully commercialize our drug candidates could be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Any of the foregoing could have a material adverse effect on our business.

Changes in patent law in the United States and in non-U.S. jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our drug candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity, and therefore is costly, time-consuming and inherently uncertain. Past or future patent reform legislation in the United States and other countries could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents, may diminish the value of our patents or narrow the scope of our patent protection and may affect the scope, strength and enforceability of our patent rights or the nature of proceedings that may be brought by or against us related to our patent rights. Under the Leahy-Smith America Invents Act (America Invents Act), enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted and may also affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to challenge the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings.

Additionally, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on decisions by the U.S. Congress, the U.S. federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Any of the foregoing, including any similar adverse changes in the patent laws of other jurisdictions, could also have a material adverse effect on our business, financial condition, results of operations and prospects.

Even if we are able to obtain patent protection for our drug candidates, the life of such protection, if any, is limited, and third parties could develop and commercialize products and technologies similar or identical to ours and compete directly against us after the expiration of our patent rights, if any, and our ability to successfully commercialize any product or technology would be materially adversely affected.

The life of a patent and the protection it affords is limited. For example, in the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non provisional filing date. Even if we successfully obtain patent protection for an approved drug candidate, it may face competition from generic or biosimilar medications. Manufacturers of generic or biosimilar drugs may challenge the scope, validity or enforceability of our patents in court or before a patent office, and we may not be successful in enforcing or defending those intellectual property rights and, as a result, may not be able to develop or market the relevant product exclusively, which would materially adversely affect any potential sales of that product.

Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such drug candidates might expire before or shortly after such drug candidates are commercialized. As a result, our patents and patent applications may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Even if we believe we are eligible for certain patent term extensions, there can be no assurance that the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, will agree with our assessment of whether such extensions are available, and such authorities may refuse to grant extensions to our patents, or may grant more limited extensions than we request. Upon the expiration of patents that may issue from our pending patent applications, we will not be able to assert such patent rights against potential competitors and other third parties, which would materially adversely affect our business, financial condition, results of operations and prospects.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights, that are important or necessary to the development of our drug candidates. It may be necessary for us to use the patented or proprietary technology of a third party to commercialize our own technology or drug candidates, in which case we would be required to obtain a license from such third party. A license to such intellectual property may not be available or may not be available on commercially reasonable terms, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, also may be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our drug candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. We may not be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional drug candidates we may seek to acquire.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on our business.

Our commercial success depends, in part, upon our ability, and the ability of our collaborators to develop, manufacture, market and sell our drug candidates and future drug candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and other proprietary rights of third parties.

Numerous third-party U.S. and non-U.S. issued patents exist in the area of biotechnology, including in the area of targeted protein degraders and including patents owned or controlled by our competitors. There is considerable and complex intellectual property litigation in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, reexamination, and *inter partes* review proceedings before the USPTO and oppositions and other comparable proceedings in foreign jurisdictions. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our drug candidates, future drug candidates and technology, including interference, derivation, reexamination or *inter partes* review proceedings before the USPTO. Our competitors or other third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future and claims may also come from competitors or other third parties against whom our own patent portfolio may have no deterrent effect. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. Other parties may allege that our drug candidates or the use of our technologies infringe patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization.

As we continue to develop and, if approved, commercialize our current and future drug candidates, competitors or other third parties may claim that our technology infringes, misappropriates or otherwise violates their intellectual property rights. There are and may in the future be additional U.S. and foreign-issued patents and pending patent applications owned by third parties in the fields in which we are pursuing drug candidates. For example, we are aware of a patent owned by a third party with a claim that covers many potential targeted protein degraders. This patent may be alleged to cover one or more of our targeted protein degrader drug candidates, including our NX-2127 and NX-5948 drug candidates. While we believe that we have valid defenses against any assertion of such patent against us, such defenses may be unsuccessful. If we are unsuccessful and any of our targeted protein degrader drug candidates is found to infringe this patent, we could be required to obtain a license to such patent or forced to permanently cease developing, manufacturing, marketing and commercializing the infringing targeted protein degrader drug candidate. We may not be able to obtain any required license on commercially reasonable terms or at all, and even if we were able to obtain a license, it could be non-exclusive, thereby giving the licensor and other third parties the right to use the same technologies licensed to us, and it could require us to make substantial licensing, royalty and other payments. We also could be forced, including by court order, to permanently cease developing, manufacturing, marketing and commercializing the drug candidate. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willingly infringed any such patent. Even if we were ultimately to prevail, any litigation could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

Moreover, as the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our drug candidates may give rise to claims of infringement of the patent rights of others. There may be third-party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our drug candidates or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our drug candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents.

Patent and other types of the intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. If we are found, or believe there is a risk we may be found, by a court of competent jurisdiction to infringe, misappropriate or otherwise violate a third party's intellectual property rights, we could be required or may choose to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any such license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing, royalty or other payments. Without such a license, we could be forced, including by court order, to cease commercializing the infringing technology or drug candidate. In addition, we could be found liable for monetary damages, which could be significant, including treble damages and attorneys' fees if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from commercializing our drug candidates or future drug candidates or force us to cease some of our business operations, which could materially harm our business. Alternatively, we may need to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. If we lose a foreign patent lawsuit alleging our infringement of a competitor's patents, we could be prevented from marketing our therapeutics in one or more foreign countries and/or be required to pay monetary damages for infringement or royalties in order to continue marketing. Claims that we have misappropriated the confidential information, trade secrets or other intellectual property of third parties could have a similar negative impact on our business. Any of these outcomes would have a material adverse effect on our business.

Further, we do not know which processes we will use for commercial manufacture of our future products, or which technologies owned or controlled by third parties may prove important or essential to those processes. Many companies have filed, and continue to file, patent applications related to novel protein modulation therapies that target disease-causing proteins and many companies have filed and continue to file patent applications related to ACT. Some of these patent applications have already been allowed or issued and others may issue in the future. Because this area is competitive and of strong interest to pharmaceutical and biotechnology companies, there likely will be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. Furthermore, because patent applications can take many years to issue, may be confidential for 18 months or more after filing and can be revised before issuance, there may be applications now pending that we are not aware of that may later result in issued patents that may be infringed by the manufacture, use, sale or importation of our drug candidates or future products. If a patent holder believes the manufacture, use, sale, offer for sale or importation of one of our drug candidates or future products infringes its patent, the patent holder may sue us even if we have licensed other patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our licensed patent portfolio may therefore have no deterrent effect.

It is also possible that we have failed to identify all relevant third-party patents or applications. Patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale, importation or use of a current or future drug candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, later be amended in a manner that could cover our technologies, our future products or the manufacture or use of our future products.

Third parties may assert infringement claims against us based on existing intellectual property rights and intellectual property rights that may be granted in the future. If we were to challenge the validity of an issued U.S. patent in court, such as an issued U.S. patent of potential relevance to some of our drug candidates or future drug candidates or manufacture or methods of use, we would need to overcome a statutory presumption of validity that attaches to every U.S. patent. This burden is a high one and in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity or enforceability by invalidating the claims of any such U.S. patent or finding that our drug candidates or technology did not infringe any such claims.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may be time-consuming, cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities and ongoing business operations. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our future products or processes. 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, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. Unlike some of our larger competitors and other third parties, we may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. Uncertainties resulting from the litigation of patent litigation and other proceedings could delay our research and development efforts, adversely affect our ability to raise additional funds, and could limit our ability to continue our operations. Any of the foregoing could have a material adverse effect on our business.

We may be subject to claims by third parties asserting that we or our employees, consultants, contractors or advisors have misappropriated, wrongfully used or disclosed alleged trade secrets or other intellectual property, or claiming ownership of what we regard as our own intellectual property.

We employ individuals who were previously employed at universities as well as other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We have received confidential and proprietary information from collaborators, prospective licensees and other third parties. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's former employer. We also may in the future be subject to claims that we have caused such individual to breach the terms of his or her non-competition or non-solicitation agreement or from former employers or other third parties claiming to have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these claims. We may not be successful in defending these claims, and if we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. In addition, we may lose personnel as a result of such claims and any such litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent contractors. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our drug candidates, which would have a material adverse effect on our business, results of operations, financial condition and prospects. Even if we are successful, litigation could result in substantial cost and reputational loss and be a distraction to our management and other employees.

In addition, although it is our policy to require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Moreover, even when we obtain agreements assigning intellectual property to us, such assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Furthermore, individuals executing agreements with us may have preexisting or competing obligations to a third party, such as an academic institution, and thus an agreement with us may be ineffective in perfecting ownership of inventions developed by that individual. In addition, we or our licensors may in the future be subject to claims by former employees, consultants or other third parties asserting an ownership right in our owned or licensed patents or patent applications. An adverse determination in any such litigation or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar technology and therapeutics, without payment to us, or could limit the duration of the patent protection covering our technology and drug candidates. Such challenges may also result in our inability to develop, manufacture or commercialize our drug candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our owned or licensed patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future drug candidates. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Competitors or other third parties may infringe our patents, the patents of our licensors, or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which, regardless of merit, can be expensive, time-consuming, unpredictable and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke those parties to assert counterclaims against us alleging that we infringe their patents or other intellectual property. In addition, in a patent infringement proceeding, a court may decide that a patent of ours or our licensors is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or 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. Grounds for a validity challenge could include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description, non-enablement or failure to claim patent-eligible subject matter. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include reexamination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions. Such proceedings could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover our drug candidates or prevent third parties from competing with our drug candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we or our licensing partners were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on our drug candidates. An adverse result in any litigation or proceeding involving our patents or patent applications may put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly.

Even if we successfully assert our patents or other intellectual property rights, a court may not award remedies that sufficiently compensate us for our losses. The impact of public announcements of the results of hearings related to such awards on the price of our common stock may be uncertain. If securities analysts or investors perceive such results to be negative, it could have a substantial adverse effect on the price of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Some of our competitors or other third parties may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel for significant periods of time during such litigation could outweigh any benefit we receive as a result of the proceedings. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing, misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may not be able to protect our intellectual property rights and to secure patent term extensions throughout the world.

Filing, prosecuting and defending patents on drug candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In some cases, we may not be able to obtain patent protection for certain technology and drug candidates outside the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, even in jurisdictions where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we do pursue patent protection, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors or other third parties may use our technologies in jurisdictions where we have not pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our drug candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents, if pursued and obtained, 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 costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our business, financial condition, results of operations and prospects could be materially and adversely affected.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by governmental patent offices, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance, renewal and annuity fees and various other government fees on any issued patent are due to be paid to the USPTO and patent offices in foreign countries in several stages over the lifetime of the patent. The USPTO and patent offices in various foreign countries require compliance with a number of procedural, documentary, fee payment and other similar requirements during the patent application process. Although 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 a patent or 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. In such an event, our competitors or other third parties might be able to enter the market, which would have a material adverse effect on our business.

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 drug candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, and confidentiality agreements to maintain our competitive position. However, trade secrets can be difficult to protect. We seek to protect our trade secrets, proprietary technology and processes, 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, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. 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 inside and outside of the United States are less willing or unwilling to protect trade secrets. As a result, we could lose our trade secrets and third parties could use our trade secrets to compete with our drug candidates and technology.

We cannot guarantee that we have entered into such agreements with each party that may have or had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems; however, such systems and security measures may be breached, and we may not have adequate remedies for any breach.

Moreover, our competitors or other third parties may independently develop knowledge, methods and know-how equivalent to our trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third parties, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third parties, our competitive position would be harmed.

Intellectual property rights do not necessarily address all potential threats.

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

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

- it is possible that our pending owned patent applications or those that we may own or license in the future will not lead to issued patents;
- issued patents that we may hold rights to in the future may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

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

Risks Related to Regulatory Approval and Marketing of Our Drug Candidates

The regulatory approval process of the FDA is lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to obtain marketing approval for our drug candidates, our business will be substantially harmed.

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

Our drug candidates could be delayed or fail to receive marketing approval for many reasons, including the following:

- the FDA may disagree with our interpretation of data from preclinical studies or clinical trials;
- the FDA may disagree with the design or implementation of our planned clinical trials;
- data collected from clinical trials of our drug candidates may not be sufficient to support the submission of an NDA to the FDA or other submissions necessary to obtain marketing approval in the United States;
- we may be unable to demonstrate to the satisfaction of the FDA that a drug candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA for approval;
- we may be unable to demonstrate that our drug candidates' clinical and other benefits outweigh their safety risks;
- the FDA may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain regulatory approval to market any of our drug candidates, which would significantly harm our business, results of operations, financial condition and prospects. The FDA has substantial discretion in the approval process, and in determining when or whether regulatory approval will be obtained for any of our drug candidates. Even if we believe the data collected from clinical trials of our drug candidates are promising, such data may not be sufficient to support approval by the FDA.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, or they may impose significant limitations in the form of narrow indications, warnings or a risk evaluation and mitigation strategy (REMS). In addition, regulatory authorities may not approve the price we intend to charge for our products, may require precautions or contra-indications with respect to conditions of use, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates.

We may submit an NDA for our drug candidates under the Accelerated Approval Pathway. If we are unable to obtain approval of our drug candidates through the Accelerated Approval Program in the United States, we may be required to conduct additional nonclinical and clinical studies and trials beyond those that we currently contemplate, which could increase the expense of obtaining, reduce the likelihood of obtaining and/or delay the timing of obtaining, necessary marketing approval. Even if we receive approval from the FDA through the Accelerated Approval Program, if our confirmatory postmarketing trial does not verify clinical benefit, or if we do not comply with rigorous postmarketing requirements, the FDA may seek to withdraw the approval.

We may submit an NDA for one or more of our drug candidates seeking approval through the Accelerated Approval pathway. For any approval to market a drug product, we must provide the FDA and foreign regulatory agencies with clinical data that adequately demonstrate the safety and efficacy of the product for the indication applied for in the NDA or other respective regulatory filings. The Accelerated Approval Program is one of several approaches used by the FDA to make prescription drugs more rapidly available for the treatment of serious or life-threatening diseases. Section 506(c) of the Federal Food, Drug and Cosmetic Act (FDCA) provides that the FDA may grant accelerated approval to "a product for a serious or life-threatening condition upon a determination that the product has an effect on 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, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments." Approval through the Accelerated Approval Program is subject, however, to the requirement that the applicant conduct additional postmarketing clinical trials to verify and describe the drug's clinical benefit, where there is uncertainty as to the relationship of the surrogate endpoint to the clinical benefit, or of the observed clinical endpoint to ultimate outcome. Typically, clinical benefit is verified when postmarketing clinical trials show that the drug provides a clinically meaningful positive therapeutic effect, that is, an effect on how a patient feels, functions, or survives. If such confirmatory postmarketing trial fails to confirm the drug's clinical profile or risks and benefits, the FDA may withdraw its approval of the drug.

The FDA has broad discretion with regard to approval through the Accelerated Approval Program, and even if we believe that the Accelerated Approval Program is appropriate for one of our drug candidates, we cannot assure you that the FDA will ultimately agree. Furthermore, even if we do obtain approval through the Accelerated Approval Program, we may not experience a faster development process, review or approval compared to conventional FDA procedures.

Even if the FDA reviews an NDA seeking accelerated approval, there can be no assurance that approval will be granted on a timely basis, or at all. The FDA may disagree that the design of, or results from, our studies support accelerated approval. Additionally, the FDA could require us to conduct further studies or trials prior to granting approval of any type, including by determining that approval through the Accelerated Approval Program is not appropriate and that our clinical trials may not be used to support approval through the conventional pathway. We might not be able to fulfill the FDA's requirements in a timely manner, which would cause delays, or approval might not be granted because our submission is deemed incomplete by the FDA. There also can be no assurance that after subsequent FDA feedback we will continue to pursue approval through the Accelerated Approval Program. A failure to obtain approval through the Accelerated Approval Program could result in a longer time period to obtain approval of our drug candidates, could increase the cost of their development, could delay our ability to commercialize our products and could significantly harm our financial position and competitive position in the marketplace.

Even if we receive approval for one or more of our drug candidates through the Accelerated Approval Program, we will be subject to rigorous postmarketing requirements, including the completion of one or more confirmatory postmarketing trials as the FDA may require, to verify the clinical benefit of the product, and submission to the FDA of all promotional materials prior to their dissemination. The FDA could seek to withdraw the approval for multiple reasons, including if we fail to conduct any required confirmatory postmarketing trial with due diligence, our confirmatory postmarketing trial does not confirm the predicted clinical benefit, other evidence shows that the product is not safe or effective under the conditions of use, or we disseminate promotional materials that are found by the FDA to be false and misleading.

Moreover, Congress is considering potential changes to the Accelerated Approval Program that could impact our ability to obtain accelerated approval, or increase the burdens associated with postmarketing requirements in the event we do obtain accelerated approval. It is not possible to predict which changes Congress will include if it decides to enact changes to the Accelerated Approval Program, or if Congress will make any changes to the Accelerated Approval Program at all.

Any delay in obtaining, or inability to obtain, approval through the Accelerated Approval Program, or any issues in maintaining approval granted under the Accelerated Approval Program, would delay or prevent commercialization of our products, and would materially adversely affect our business, financial condition, results of operations and prospects.

We, as a company, have limited experience in filing for and obtaining regulatory approval to initiate a clinical trial and we do not have experience completing any clinical trials, including large-scale, pivotal clinical trials or in manufacturing or in quality assurance in order to market a new drug in the United States or in any other jurisdiction.

As a company, we have limited experience in filing for or obtaining regulatory approval to initiate clinical trials, we do not have experience completing any clinical trials, including large-scale, pivotal clinical trials and we rely on third parties to conduct our clinical trials. We also do not have experience in manufacturing or in quality assurance in order to market a new drug and expect to rely on CROs or other third-party consultants or vendors to assist us in this process. Our inexperience may result in failure to or delays in obtaining the required regulatory approvals to initiate clinical trials, to successfully complete clinical trials and to obtain marketing approval for our drug candidates. If we are unable to obtain regulatory and marketing approval for our drug candidates or experience significant delays in our efforts to do so, our business could be substantially harmed.

Failure to obtain marketing approval in foreign jurisdictions would prevent our drug candidates from being marketed abroad and may limit our ability to generate revenue from product sales.

To market and sell our drug candidates in jurisdictions outside the United States, we must obtain separate 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 approvals from foreign regulatory authorities 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, we must secure product reimbursement approvals before regulatory authorities will approve the product for sale in that country. Failure to obtain foreign regulatory approvals on a timely basis or non-compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our drug candidates in certain countries. 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. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any jurisdiction, which would materially impair our ability to generate revenue.

The UK's exit from the EU continues to create political and economic uncertainty, particularly in the UK and the EU. The UK is now being treated as a 'third country' by the EU and new UK legislation has taken effect. This means that some regulatory activities, such as batch testing and Qualified Person certification, conducted in Great Britain are no longer recognized in the EU. However, the UK and EU have concluded a Trade and Cooperation Agreement (TCA), which has been approved by the UK Parliament, European Council and European Parliament and has limited the disruption to the supply of medicines, particularly by enabling tariff and quota-free trade between the UK and the EU (provided that the rules of origin requirements are met), and has streamlined some issues, for example by enabling mutual recognition of cGMP inspections and certificates. The regulatory framework for medicines that existed before the end of the transition period has also effectively been preserved in UK domestic legislation as 'retained EU law.' By retaining a snapshot of EU legislation at its core, the UK has prevented substantial divergence in the regulation of medicines (although divergence has appeared in some areas). However, some changes to the UK legislation have been immediately necessary, including the implementation of the Northern Ireland Protocol (NIP), pursuant to which, the EU pharmaceutical legal framework acquis continues to apply in Northern Ireland (subject to periodic consent of the Northern Ireland Legislative Assembly), and only products compliant with EU law can be placed in the Northern Ireland market—adding an extra layer of regulatory complexity. As a result, companies now need to comply with a separate UK regulatory legal framework in order to commercialize medicinal products in Great Britain (namely, England, Wales and Scotland, as EU law continues to apply in Northern Ireland). The UK government has attempted to renegotiate fundamental aspects of the NIP so this is an unpredictable area for companies in the near future. Failed attempts to renegotiate the NIP have led to media reports of the UK potentially triggering Article 16 of the NIP, a safeguarding measure, that may be engaged unilaterally if the application of the NIP leads to serious economic, societal or environmental difficulties that are liable to persist, or to diversion of trade. Currently, the UK government has introduced a bill 'Northern Ireland Protocol Bill' which if enacted into law would enable the government to unilaterally disapply parts of the NIP which may lead to changes to the regulatory environment in Northern Ireland, and may trigger retaliatory measures against the UK by the European Union. The TCA allows for future deviation from the current regulatory framework and it is not known if and/or when any deviations may occur, which may have an impact on development, manufacture, marketing authorization, commercial sales and distribution of pharmaceutical products. It is also important to note that obtaining a marketing authorization is not sufficient to gain effective access to the market in the EU and in the UK; companies still need to agree to a reimbursement price for the products and in some jurisdictions, such as the UK and Germany, a further positive recommendation from health technology on cost-effectiveness is required for the products to be actually prescribed and reimbursed by the respective national health systems (see "—Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues from the sales of drugs," below). If we fail to comply with the regulatory requirements in international markets and thus do not receive applicable marketing approvals, our target market will be reduced, our ability to realize the full market potential of our drug candidates will be harmed and our business will be adversely affected. We may not obtain foreign regulatory approvals on a timely basis, or at all. Our failure to obtain approval of any of our drug

candidates by regulatory authorities in another country may significantly diminish the commercial prospects of that drug candidate and our business prospects could decline.

Even if we, or any collaborators, obtain marketing approvals for our drug candidates, the terms of approvals and ongoing regulation of our products may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any collaborators, must therefore comply with requirements concerning advertising and promotion for any of our drug candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we, and any collaborators, will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA, EMA, Medicines and Healthcare products Regulatory Agency (MHRA) and other regulatory requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance, as well as the corresponding maintenance of records and documentation and reporting requirements. We, our third-party manufacturers, and any collaborators and their third-party manufacturers could be subject to periodic unannounced inspections by the FDA and other regulatory agencies to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or any collaborators, receive marketing approval for one or more of our drug candidates, we, any collaborators, and our respective third-party manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and any collaborators, are not able to comply with post-approval regulatory requirements, we, and any collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or any collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition and prospects.

Any drug candidate for which we, or any collaborators, obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market and we, or any collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our products when and if any of them are approved.

Any drug candidate for which we, or any collaborators, obtain marketing approval, as well as the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA, EMA, the MHRA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians, tracking and tracing, serialization, postmarket adverse event reporting, and recordkeeping. Even if marketing approval of a drug candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement REMS. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed. If any of our drug candidates receive marketing approval, the accompanying label may limit the approved use of our drug in this way, which could limit sales of the product.

Clinical trials of our drug candidates must be conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any future collaborator, may indicate an apparent positive effect of a drug candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If one or more of our drug candidates receives marketing approval and we, or others, discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the drug or seize the drug;
- we, or any future collaborators, may be required to recall the drug, change the way the drug is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular drug;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;

- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any future collaborators, could be sued and held liable for harm caused to patients;
- the drug may become less competitive in the marketplace; and
- our reputation may suffer.

Any of these events could have a material and adverse effect on our operations and business and could adversely impact our stock price.

The FDA also may impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product, including the adoption and implementation of REMS. The FDA and other agencies, including the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our products only for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws. Other jurisdictions, including European countries, have similar provisions which may lead to investigations and enforcement actions by national authorities.

In addition, later discovery of previously unknown side effects or other problems with our products or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions and warnings on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- suspension of any ongoing clinical trials;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; or
- litigation involving patients using our products.

Non-compliance with EU and UK requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population (as explained further under "—If any of our drug candidates are not considered to be a new active substance or are deemed to fall within the "global marketing authorization" of an existing medicinal product or if pediatric studies are not adequately completed, this may result in lack of regulatory data protection or failure to obtain an extension to existing regulatory data protection," below), also can result in significant financial penalties, and non-compliance with pediatric requirements may prevent regulatory approvals from being granted. Similarly, failure to comply with the EU and UK's requirements regarding the protection of personal information can lead to significant penalties and sanctions.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs applicable to drug manufacturers which include requirements relating to quality control and quality assurance, as well as the corresponding maintenance of records and documentation and reporting requirements. We, any contract manufacturers we may engage in the future, our collaborators and their contract manufacturers also will be subject to other regulatory requirements, including submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements regarding the distribution of samples to clinicians, recordkeeping, and costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product, such as the requirement to implement a REMS.

If we decide to seek Orphan Drug Designation or other designations from regulators for any of our current or future drug candidates, we may be unsuccessful or may be unable to maintain the benefits associated with these designations, including the potential for supplemental market exclusivity associated with an Orphan Drug Designation.

We may seek Orphan Drug Designation or other designations from regulators for one or more of our current or future drug candidates. Regulatory authorities in some jurisdictions, including the United States, EU and European Economic Area (EEA), Switzerland and the UK, may designate drugs or biological products for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug in the United States will be recovered from sales in the United States for that drug or biological product. In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. After the FDA grants Orphan Drug Designation, the identity of the drug or biological product and its potential orphan use are disclosed publicly by the FDA. Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review and licensure process.

If a product that has Orphan Drug Designation subsequently receives the first FDA approval or licensure for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including an NDA or BLA, to market the same drug or biological product for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the biological product was designated. As a result, even if one of our drug candidates receives orphan exclusivity, the FDA can still approve or license other drugs or biological products for use in treating the same indication or disease. Further, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product.

In addition, Congress is considering updates to the orphan drug provisions of the FDCA in response to a recent decision by the U.S. Court of Appeals for the Eleventh Circuit. Any changes to the orphan drug provisions could change our opportunities for, or likelihood of success in obtaining, orphan drug exclusivity and would materially adversely affect our business, results of operations, financial condition and prospects.

We may seek Orphan Drug Designation for our drug candidates in additional orphan indications in which there is a medically plausible basis for the use of these drug candidates. Even when we obtain Orphan Drug Designation, exclusive marketing rights in the United States may be limited if we seek licensure for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if we, through our manufacturer, are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. In addition, although we may seek Orphan Drug Designation for other drug candidates, we may never receive these designations.

In order to obtain orphan designation in the EEA, the product must fulfill certain challenging criteria. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as an orphan medicinal product if it meets the following criteria: (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either the prevalence of such condition must not be more than five in 10,000 persons in the EU when the application is made, or without the benefits derived from orphan status, it must be unlikely that the marketing of the medicine would generate sufficient return in the EU to justify the investment needed for its development; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000.

Products receiving orphan designation in the EU may receive 10 years of orphan market exclusivity (which can be further extended by two years if pediatric studies have been conducted in accordance with an agreed pediatric investigational plan). Applications must first satisfy the orphan designation criteria and apply for orphan designation before making the application for marketing authorization. The applicant must then successfully maintain the orphan designation at the time of the marketing authorization application in order to qualify for 10 years of orphan market exclusivity. During this 10-year period, the competent authorities of the EU Member States and European Commission may not accept applications or grant marketing authorization for other similar medicinal products for the same orphan therapeutic indication. The protection afforded by orphan market exclusivity in the EU may, in some circumstances, be circumvented by competitor products which are demonstrated not to be 'similar' or which are authorized for different therapeutic indications. There may be a risk that products may be prescribed 'off-label' for the orphan therapeutic indication by healthcare professions in some EU Member States.

There are also three exceptions to the orphan market exclusivity principle. Marketing authorization may be granted to a similar medicinal product for the same orphan therapeutic indication if:

- the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- the holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- the holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

An orphan product can also obtain an additional two years of orphan market exclusivity in the EU if the marketing authorization application contains the results of all pediatric studies conducted in accordance with and agreed pediatric investigation plan. The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation; for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity.

The UK's regulatory legal framework provides for similar periods of protection (namely regulatory data protection, marketing protection and market exclusivity).

It is important to note that the regulatory protection afforded to medicinal products such as data exclusivity, marketing protection, market exclusivity for orphan indications and pediatric extension are currently under review at the EU level. It is expected that the protection currently afforded in the EU will be reduced in the years to come.

In addition, we filed for and received an Innovation Passport designation for NX-1607 in the UK in February 2022. The Innovation Passport is the mandated entry point to the Innovative Licensing and Access Pathway (ILAP) in the UK to facilitate approval of and market access to an innovative medicine. Grant of the Innovation Passport paves the way for enhanced engagement with key stakeholders such as the MHRA, health technology agencies in the UK such as the National Institute for Health and Care Excellence (NICE) or the Scottish Medicines Consortium (SMC) and NHS England. However, although the goal of ILAP and the Innovation Passport is to reduce the time to market and enable earlier patient access, it does not accelerate conduct of clinical trials or mean that the regulatory requirements are less stringent, nor does it ensure that any NX-1607 MAA will be approved or that any approval will be granted within any particular timeframe. Despite receiving an Innovation Passport designation, we may decide to delay or forego the commercialization of NX-1607 in the UK or the development may otherwise not proceed.

If the FDA or comparable foreign regulatory authorities approve generic versions of any of our drug candidates that receive marketing approval, or such authorities do not grant our drug candidates appropriate periods of data or market exclusivity before approving generic versions of our drug candidates, the sales of our drug candidates could be adversely affected.

Once an NDA is approved, the drug covered thereby becomes a "reference-listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations." Manufacturers may seek marketing approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications (ANDAs) in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials demonstrating safety and efficacy. Rather, the applicant generally must show that its drug is pharmaceutically equivalent to the reference listed drug, in that it has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug, and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic drugs may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic drugs are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug is typically lost to the generic drug.

The FDA may not approve an ANDA for a generic drug until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another version of such drug candidate where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug candidate. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drug candidates containing the original active agent for other conditions of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. Manufacturers may seek to launch these generic drugs following the expiration of the marketing exclusivity period, even if we still have patent protection for our drug.

Competition that our drug candidates may face from generic versions of our drug candidates could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those drug candidates. Our future revenues, profitability and cash flows could also be materially and adversely affected and our ability to obtain a return on the investments we have made in those drug candidates may be substantially limited if our drug candidates, if and when approved, are not afforded the appropriate periods of non-patent exclusivity.

If any of our drug candidates are not considered to be a new active substance or are deemed to fall within the "global marketing authorization" of an existing medicinal product or if pediatric studies are not adequately completed, this may result in lack of regulatory data protection or failure to obtain an extension to existing regulatory data protection.

Where an applicant for a marketing authorization submits a full dossier containing its own pharmaceutical, pre-clinical tests and clinical trials data, and where the application does not fall within the 'global marketing authorization' of an existing medicinal product, the applicant is entitled to eight years of regulatory data protection upon grant of the marketing authorization (the period starts to run from the first marketing authorization in the EU and EEA). During this period, applicants for approval of generics or biosimilars cannot rely on data contained in the marketing authorization dossier submitted for the already authorized, or reference, medicinal product to support their application. After the expiration of the eight-year period of regulatory data protection, the reference medicinal product benefits from a further two-year period of marketing protection. During these two years of marketing protection, no generic or biosimilar medicinal product that relies upon the reference medicinal product's dossier may be placed on the EU market, but a generic or biosimilar marketing authorization application can be submitted to the competent regulatory authorities in the EU Member States during this time. The two-year period of marketing protection can further be extended by one year if, during the first eight years of the grant of the first marketing authorization, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, even if a compound is considered to be a new active substance and the innovator is able to gain the period of regulatory data protection and marketing protection, provided that no other IP or regulatory exclusivities applied, another unrelated company could also apply for a marketing authorization and market another competing medicinal product for the same therapeutic indication if such company obtained its own marketing authorization based on a separate marketing authorization application based on a full self-standing scientific data package supporting the application. The period of regulatory data protection and marketing protection applies in the UK (running from the date of the first authorization in Great Britain).

In the EU, pursuant to Regulation 1901/2006, and in the UK pursuant to the Human Medicines Regulations 2012 (as amended), marketing authorization applications must include pediatric data based on pediatric investigation plans agreed with the EMA if the MAA concerns (i) a new active substance, or (ii) a new indication, pharmacological form, or route of administration (where the product is protected by a supplementary protection certificate or a patent qualifying for a supplementary certificate). Applicants may obtain waivers or deferrals to these requirements in certain circumstances (for example a waiver may be obtained if the condition only occurs in adult populations). Where required, pediatric studies must cover all sub-sets of the pediatric population for both existing and new indications, pharmacological forms and route of administrations. Limited further exclusions apply, including in relation to generic or biosimilar applications. Certain rewards may be available for completion of pediatric studies. For example, where MAAs include the results of all studies conducted in compliance with an agreed pediatric investigation plan, the holder of the patent or supplementary protection certificate may be entitled to a six-month extension to the supplementary protection certificate.

Our operations and relationships with actual and potential customers, providers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to penalties including criminal sanctions, civil penalties, exclusions from government programs, contractual damages and reputational harm, and could diminish our future profits and earnings.

Our arrangements with third-party payors, physicians, and other potential customers will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drug candidates for which we obtain marketing approval.

Applicable U.S. federal and state and non-U.S. healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, a criminal law, which prohibits, among other things, persons and entities from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, in cash or in kind, to induce or reward purchasing, leasing, ordering, or arranging for, referring, or recommending the purchase, lease or order of any good or service for which payment may be made, in whole or in part, under federal healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations of the federal Anti-Kickback Statute can result in significant civil monetary penalties and criminal fines, as well as imprisonment and exclusion from participation in federal healthcare programs;
- the federal civil False Claims Act, which may be enforced through civil whistleblower or *qui tam* actions and imposes significant civil penalties, treble damages and potential exclusion from federal healthcare programs against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or for making a false record or statement material to an obligation to pay the federal government or for knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Further, a violation of the federal Anti-Kickback Statute can serve as a basis for liability under the federal civil False Claims Act. There is also the federal Criminal False Claims Act, which is similar to the federal Civil False Claims Act and imposes criminal liability on those that make or present a false, fictitious or fraudulent claim to the federal government;
- the federal Civil Monetary Penalties Law, which authorizes the imposition of substantial civil monetary penalties against an entity that engages in activities including, among others (1) knowingly presenting, or causing to be presented, a claim for services not provided as claimed or that is otherwise false or fraudulent in any way; (2) arranging for or contracting with an individual or entity that is excluded from participation in federal health care programs to provide items or services reimbursable by a federal health care program; (3) violations of the federal Anti-Kickback Statute; or (4) failing to report and return a known overpayment;
- federal criminal statutes created by the Health Insurance Portability and Accountability Act (HIPAA), which impose criminal liability for, among other things, knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program, including private insurance plans, or, in any matter involving a healthcare benefit program, for knowingly and willfully making materially false, fictitious or fraudulent statements in connection with the delivery of or payment for health care benefits;
- HIPAA, as amended by HITECH, and its implementing regulations, which also imposes obligations, including mandatory contractual terms, on certain types of people and entities with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Food, Drug, and Cosmetic Act which among other things, strictly regulates drug marketing, prohibits manufacturers from marketing such products for off-label use or misbranding or adulterating their products, and regulates the distribution of samples;
- the federal and state laws that require pharmaceutical manufacturers to report certain calculated product pricing metrics to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of product coverage and reimbursement under federal healthcare programs
- the federal Physician Payment Sunshine Act, which requires applicable manufacturers of covered drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, among others, to annually track and report payments and other transfers of value provided to U.S.-licensed physicians, teaching hospitals, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse-midwives as well as certain ownership and investment interests held by physicians and their immediate families;

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, that may apply to our business practices, including sales or marketing arrangements and claims involving healthcare items or services reimbursed by 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 relevant compliance guidance promulgated by the federal government;
- state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures;
- other state laws that prohibit various marketing-related activities, such as the provision of certain kinds of gifts or meals; require the reporting of certain pricing information, including information pertaining to and justifying price increases, or prohibit prescription drug price gouging; and certain state and local laws that require the registration of pharmaceutical sales representatives; and
- state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations 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 regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of drug candidates from government-funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, 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 not to be in compliance with applicable laws, they may also be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action for an alleged or suspected violation can cause us to incur significant legal expenses and divert management's attention from the operation of the business, even if such action is successfully defended.

Providing benefits or advantages to induce or reward improper performance generally to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the EU and the UK. The provision of benefits or advantages to induce or reward improper performance is governed by the national anti-bribery laws of EU Member States, and in respect of the UK, the Bribery Act 2010. Infringement of these laws may result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, provides that, where medicinal products are being promoted to healthcare professionals, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such individuals unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision was transposed into the Human Medicines Regulations 2012 and as such remains applicable in the UK.

Payments made to physicians in certain EU Member States must be publicly disclosed. In addition, agreements with healthcare professionals must often be the subject of prior notification and approval by the healthcare professional's employer, his or her competent professional organization and/or the regulatory authorities of individual EU Member States. These requirements are set out in national laws, industry codes or professional codes of conduct, applicable in the EU Member States and in the UK. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad.

Current and future legislation may increase the difficulty and cost for us, and any collaborators, to obtain marketing approval of and commercialize our drug candidates and affect the prices we, or they, may obtain.

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 drug candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any drug candidates for which we obtain marketing approval. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any FDA-approved product.

Healthcare reform measures that may be adopted in the future, may result in reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation and regulation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient support programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. For example, included in the Consolidated Appropriations Act of 2021 were several drug price reporting and transparency measures, such as a new requirement for certain Medicare plans to develop tools to display Medicare Part D prescription drug benefit information in real time and for group and health insurance issuers to report information on pharmacy benefit and drug costs to the Secretaries of the Departments of Health and Human Services, Labor and the Treasury. Additionally, on February 2, 2022, the Biden administration signaled its continued commitment to the Cancer Moonshot initiative, which was initially launched in 2016. In its announcement, the administration noted that its new goals under the initiative include addressing inequities in order to ensure broader access to cutting-edge cancer therapeutics and investing in a robust pipeline for new treatments.

Most recently, on August 16, 2022, President Biden signed into law the Inflation Reduction Act of 2022 (the Act), which, among other provisions, included several measures intended to lower the cost of prescription drugs and related healthcare reforms. Specifically, the Act authorizes and directs the Department of Health and Human Services to set drug price caps for certain high-cost Medicare Part B and Part D qualified drugs, with the initial list of drugs to be selected by September 1, 2023, and the first year of maximum price applicability to begin in 2026. The Act further authorizes the Department of Health and Human Services to penalize pharmaceutical manufacturers that increase the price of certain Medicare Part B and Part D drugs faster than the rate of inflation. Finally, the Act creates significant changes to the Medicare Part D benefit design by capping Part D beneficiaries' annual out-of-pocket spending at $2,000 beginning in 2025. We cannot be sure whether additional legislation or rulemaking related to the Act will be issued or enacted, or what impact, if any, such changes will have on the profitability of any of our drug candidates, if approved for commercial use, in the future.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing. These include legislation and regulations regarding price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, legislative action designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

Legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our drug candidates, if any, may be. Increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues from the sales of drugs, if any.

In some countries, particularly the countries of the EU and the UK, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we, or our collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our drug to other available therapies. Furthermore, in some European countries, the authorities conduct an HTA to assess the cost-effectiveness of the product (in the UK that HTA assessment is conducted by the National Institute for Health and Care Excellence), which may significantly impact effective access to the market. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Risks Related to Employees, Managing our Growth and Other Legal Matters

The COVID-19 pandemic may adversely affect our business and the market price of our common stock.

The ongoing global pandemic of COVID-19 is impacting worldwide economic activity and poses the risk that we or our employees, contractors, suppliers, and other partners may be prevented from conducting business activities for an indefinite period of time, including due to shutdowns that may be requested or mandated by governmental authorities. Although it is not possible at this time to estimate the impact that COVID-19 could have on our business, the continued spread of COVID-19 and the measures taken by the governments of countries affected could disrupt the supply chain and the manufacture or shipment of both drug substance and finished drug product for our drug candidates for preclinical testing and clinical trials, cause diversion of healthcare resources away from the conduct of preclinical and clinical trial matters to focus on pandemic concerns, limit travel in a manner that interrupts key trial activities, such as trial site initiations and monitoring, delay regulatory filings with regulatory agencies in affected areas or adversely affect our ability to obtain regulatory approvals. Additionally, disruptions at the FDA, the EMA and other regulators, caused by global health concerns, including the COVID-19 pandemic, including delays in inspections of clinical trial or manufacturing sites required as part of the drug application review process, could result in delays of reviews and approvals of our drug candidates or our proposed clinical trials. For example, in response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products inspections of domestic manufacturing facilities through April 2020. On March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials. On July 10, 2020, the FDA announced that it is working toward the goal of restarting on-site inspections it deems to be "mission critical." On August 19, 2020, the FDA published guidance clarifying how it intends to conduct inspections during the COVID-19 pandemic, including how it plans to determine which inspections are "mission critical," and published an updated form of this guidance on May 17, 2021. Additionally, on April 14, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites. According to the guidance, the FDA intends to request such remote interactive evaluations in situations where an in-person inspection would not be prioritized, deemed mission-critical, or where direct inspection is otherwise limited by travel restrictions, but where the FDA determines that remote evaluation would still be appropriate. The FDA has since adjusted its inspection activities in response to the ongoing COVID-19 pandemic. On December 29, 2021, the FDA implemented temporary changes to its inspectional activities to ensure the safety of its employees and regulated firms. On February 2, 2022, the FDA announced that it would resume domestic surveillance inspections across all product areas on February 7, 2022. We cannot predict whether, and when, the FDA will decide to pause or resume inspections due to the COVID-19 pandemic. Moreover, it is unclear how the FDA's policies and guidance will impact any inspections of our facilities, including our clinical trial sites. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic.

The COVID-19 pandemic and mitigation measures also may have an adverse impact on global economic conditions, which could adversely impact our business, financial condition or results of operations. Additionally, the COVID-19 pandemic has resulted in significant financial market volatility and uncertainty. A continuation or worsening of the levels of market disruption and volatility seen in the recent past as a result of the COVID-19 pandemic could have an adverse effect on our ability to access capital and on the market price of our common stock. It is currently not possible to predict how long the COVID-19 pandemic and its effects will last or the time that it will take for economic activity to return to prior levels. The extent to which the COVID-19 pandemic impacts our results will depend on future developments that are highly uncertain and cannot be predicted, including new information that may emerge concerning the severity of the virus and the actions taken to contain its impact. See also the section titled "—Risks Related to Dependence on Third Parties."

If we fail to attract and retain management and other key personnel, we may be unable to continue to successfully develop our current and any future drug candidates, commercialize our drug candidates or otherwise implement our business plan.

Our ability to compete in the highly competitive pharmaceuticals industry depends upon our ability to attract and retain highly qualified managerial, scientific, medical, sales and marketing and other personnel. We are highly dependent on our management and scientific personnel, including our President and Chief Executive Officer, Arthur T. Sands, M.D., Ph.D., our Chief Scientific Officer, Gwenn Hansen, Ph.D., and our Chief Operating Officer and Executive Vice President of Product Development, Stefani A. Wolff. The loss of the services of Dr. Sands, Dr. Hansen or Ms. Wolff or other members of our senior leadership team could impede, delay or prevent the successful development of our product pipeline, completion of our current and planned clinical trials, commercialization of our products or in-licensing or acquisition of new assets, and could negatively impact our ability to successfully implement our business plan. If we lose the services of such individuals, we might not be able to find suitable replacements on a timely basis or at all, and our business could be harmed as a result. We do not maintain "key man" insurance policies on the lives of these individuals or the lives of any of our other employees.

We employ all of our executive officers and key personnel on an at-will basis and their employment can be terminated by us or them at any time, for any reason and without notice. In order to retain valuable employees at our company, in addition to salary and cash incentives, we provide stock options and restricted stock units (RSUs) that vest over time. The value to employees of stock options and RSUs that vest over time will be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract offers from other companies.

Moreover, we might not be able to attract or retain qualified management and other key personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Francisco Bay Area where we are headquartered. We could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts. Many pharmaceutical companies with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. If we are not able to attract and retain the necessary personnel to accomplish our business objectives, we may experience constraints that will harm our ability to implement our business strategy and achieve our business objectives.

In addition, we have scientific and clinical advisors who assist us in formulating our development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

We will need to grow our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As our development and commercialization plans and strategies develop, and as we continue our transition into operating as a public company, we expect to expand our employee base for managerial, operational, financial and other resources. In addition, we have limited experience in product development. We filed our first IND in December 2020 and currently have four drug candidates in ongoing Phase 1 trials. As our drug candidates enter and advance through preclinical studies and clinical trials, we will need to expand our development, regulatory and manufacturing capabilities or contract with other organizations to provide these capabilities for us. In the future, we expect to have to manage additional relationships with collaborators or partners, suppliers and other organizations. Our ability to manage our operations and 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.

Our employees, independent contractors, vendors, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading laws.

We are exposed to the risk that our employees, independent contractors, vendors, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include:

- intentional, reckless or negligent conduct or disclosure to us of unauthorized activities that violate the regulations of the FDA or similar foreign regulatory authorities;
- healthcare fraud and abuse in violation of U.S. and foreign laws and regulations;
- violations of U.S. federal securities laws relating to trading in our common stock; and
- failures to report financial information or data accurately.

In particular, 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 regulate a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. While we have adopted a code of conduct and implemented other internal controls applicable to all of our employees, 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. Additionally, we are subject to the risk that a person could allege 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, including the imposition of civil, criminal and administrative penalties, damages, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, diminished profits and future earnings, any of which could adversely affect our ability to operate our business or cause reputational harm.

We depend on our information technology systems, and any failure of these systems, or those of our CROs, third-party vendors, collaborators or other contractors or consultants we may utilize, could harm our business. Security breaches, cyber-attacks, loss of data, and other disruptions could compromise sensitive information related to our business or other personal information, prevent us from accessing critical information and expose us to liability, which could adversely affect our business, reputation, results of operations, financial condition and prospects.

We collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems, infrastructure and data to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including but not limited to intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We have established physical, electronic and organizational measures to safeguard and secure our systems which are designed to prevent data compromise, and rely on commercially available systems, software, tools and monitoring to provide security for our information technology systems and the processing, transmission and storage of digital information. We have also outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors may or could have access to our confidential information.

Despite the implementation of security measures, our internal information technology systems and infrastructure, and those of our current and any future collaborators, contractors and consultants and other third parties on which we rely, are vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet (including harmful attachments to emails, ransomware, denial-of-service attacks, social engineering, and other means to affect service reliability and threaten the confidentiality, integrity, and availability of information), persons inside our organization, or persons with access to systems inside our organization. Any of the foregoing may compromise our system infrastructure, or that of our third-party vendors and other contractors and consultants or lead to data leakage.

The risk of a security breach or disruption, particularly through cyber-attacks or cyber-intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. We may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources. In addition, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information or other intellectual property. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or those of our third-party vendors and other contractors and consultants, or inappropriate disclosure of confidential or proprietary information, we could incur liability and reputational damage and the further development and commercialization of our drug candidates could be delayed. The costs to us to mitigate network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be material, and although we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. If the information technology systems of our third-party vendors and other contractors and consultants become subject to disruptions or security breaches, we may have insufficient recourse against such third parties and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring.

We and our third-party service providers regularly defend against and respond to data security incidents, and we cannot assure you that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, breaches in our systems, or those of our third-party vendors and other contractors and consultants, or other cyber incidents that could have a material adverse effect upon our reputation, business, operations, or financial condition. If such an event were to occur that causes interruptions in our operations, or those of our third-party vendors and other contractors and consultants, it could result in a material disruption or delay of our product development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our internal information technology systems or those of our third-party vendors and other contractors and consultants, or security breaches could result in the loss, misappropriation, and/or unauthorized access, use, or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information, and personal information), which could result in financial, legal, business, and reputational harm to us. If any such event, including a computer security breach, results in the unauthorized access, use or release of personally identifiable information, our reputation could be materially damaged. In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to various federal and state privacy and security laws (and other similar non-U.S. laws), subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. For example, data breaches frequently result in regulatory actions and commercial and class action litigation based on a variety of laws and legal duties, such as the California Consumer Privacy Act (CCPA), which provides for a private right of action in the event of certain data security breaches. Such actions could result in significant legal and financial exposure and reputational damages that could have a material adverse effect on our business, financial condition, results of operations and prospects.

We are or may become subject to a variety of stringent privacy and data security laws, regulations, policies and contractual obligations related to data privacy and security, and changes in such laws, regulations, policies and contractual obligations and our failure, or any failure by our third-party vendors, collaborators, contractors or consultants, to comply with them could harm our business and result in enforcement action by regulators and claims from affected individuals.

We maintain and process, and our third-party vendors, collaborators, contractors and consultants maintain and process on our behalf, a large quantity of sensitive information, including confidential business, personal and patient health information in connection with our preclinical and clinical studies and our employees, and are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information. Failure by us or our third-party vendors, collaborators, contractors and consultants to comply with any of these laws and regulations could result in enforcement action against us, including fines, imprisonment of company officials and public censure, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

In the United States, there are numerous federal and state privacy and data security laws and regulations governing the collection, use, disclosure and protection of personal information, including federal and state health information privacy laws, federal and state security breach notification laws, and federal and state consumer protection laws. Each of these laws is subject to varying interpretations and the legislative landscape is constantly evolving. In particular, laws and regulations governing the privacy of health information, such as HIPAA, establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining how protected health information may be used, shared or processed in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. Further, if we fail to comply with applicable privacy laws, we could face civil and criminal penalties, or claims for breach of contract. The U.S. Department of Health and Human Services (HHS) has enforcement discretion, and any enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

Data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect. For example, the CCPA, which came into effect on January 1, 2020, and became enforceable by the California Attorney General on July 1, 2020, along with related regulations which came into force on August 14, 2020. Additionally, although not effective until January 1, 2023, the California Privacy Rights Act (CPRA), which expands upon the CCPA, was passed in the November 2020 election. The CCPA gives (and the CPRA will give) California residents expanded privacy rights, including the right to request correction, access, and deletion of their personal information, the right to opt out of certain personal information sharing, and the right to receive detailed information about how their personal information is processed. Additionally, the CCPA requires companies that process personal information of California residents to make disclosures to consumers about their data collection, use and sharing practices, allow consumers to opt out of certain data sharing with third parties and provide a private right of action for data breaches, as described above. Although the CCPA includes limited exceptions, including exceptions for personal health information collected by covered entities or business associates subject to HIPAA, among others, the CCPA may regulate or impact our processing of personal information depending on the context. Additionally, the CPRA expands on the requirements of the CCPA by granting California residents expanded privacy rights and additional requirements for businesses. The CCPA and CPRA may increase our compliance costs and potential liability, particularly in the event of a data breach, and could have a material adverse effect on our business, including how we use personal information, financial condition, results of operations or prospects.

The CCPA has prompted a number of proposals for new federal and state-level privacy legislation. Additional states have passed privacy laws, such as the Virginia Consumer Data Protection Act, the Colorado Privacy Act, the Utah Consumer Privacy Act and the Connecticut Personal Data Privacy and Online Monitoring Act, all of which are similar to the CCPA. Such new privacy laws add additional complexity, requirements, restrictions and potential legal risk, require additional investment in resources for compliance programs, and could impact business strategies and the availability of previously useful data. The interplay of federal and state laws (e.g., in addition to California, Massachusetts and Nevada have adopted laws requiring the implementation of certain security measures to protect personal information, and all 50 states and the District of Columbia, Puerto Rico, the U.S. Virgin Islands and Guam have adopted breach notification laws) may be subject to varying interpretations by courts and government agencies, creating complex compliance issues for us and our customers and potentially exposing us to additional expense, adverse publicity and liability. Further, as regulatory focus on privacy, security and data use issues in the U.S. continues to increase and laws and regulations concerning the protection of personal information expand and become more complex, these potential risks to products and services could intensify.

In addition, in May 2018, the EU General Data Protection Regulation (EU GDPR) took effect in the EEA. The EU GDPR governs the collection, use, disclosure, transfer or other processing of personal data, replacing data protection laws issued by each EU member state based on the Directive 95/46/EC (Directive). The EU GDPR imposes additional compliance burdens, including by mandating burdensome documentation requirements and granting certain privacy rights to individuals to control how companies collect, use, disclose, retain and otherwise process information about them as well as changes to informed consent practices, the obligation to appoint data protection officers in certain circumstances, the obligation to notify relevant data supervisory authorities of personal data breaches without undue delay (and no later than 72 hours) after becoming aware of the personal data breach, and the requirement for more detailed notices for clinical trial subjects and investigators. In addition, the EU GDPR increases the scrutiny of transfers of personal data from clinical trial sites and other third parties (e.g. CROs) located in the EEA to the United States and other jurisdictions that the European Commission does not recognize as having "adequate" data protection laws. In particular, on July 16, 2020, the Court of Justice of the EU (Court of Justice) in *Schrems II* invalidated the European Union-United States (EU-U.S.) Privacy Shield on the grounds that the EU-U.S. Privacy Shield failed to offer adequate protections to EU personal information transferred to the United States. While the Court of Justice upheld the use of other data transfer mechanisms, such as the Standard Contractual Clauses, the decision has led to some uncertainty regarding the use of such mechanisms for data transfers to the United States, and the Court of Justice made clear that reliance on Standard Contractual Clauses alone may not necessarily be sufficient in all circumstances. The use of Standard Contractual Clauses for the transfer of personal information specifically to the United States also remains under review by a number of European data protection supervisory authorities. For example, German and Irish supervisory authorities have indicated that the Standard Contractual Clauses alone provide inadequate protection for EU-U.S. data transfers. Use of the data transfer mechanisms must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals. The European Data Protection Board issued additional guidance regarding international transfers which may require us to implement additional safeguards to further enhance the security of data transferred out of the EEA, which could increase our compliance costs, expose us to further regulatory scrutiny and liability, and adversely affect our business. In March 2022, U.S. and EU authorities announced a new Trans-Atlantic Data Privacy Framework to replace the invalidated Privacy Shield, but it is not clear what the ultimate requirements will be, or when it will be available for participation. In the meantime, the European Commission published new versions of the Standard Contractual Clauses in June 2021 which place onerous obligations on the parties. The EU GDPR imposes substantial fines for breaches and violations (up to the greater of €20 million or 4% of our global turnover). The EU GDPR allows data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the EU GDPR.

Further, following the end of the Brexit Transition Period (on December 31, 2020) the EU GDPR has been implemented in the UK (as the UK GDPR)—non-compliance with which may lead to similar compliance and operational costs as the EU GDPR with potential fines of up to £17 million or 4% of global turnover. The UK GDPR sits alongside the UK Data Protection Act 2018 which implements certain derogations in the EU GDPR into UK law. Under the UK GDPR, companies not established in the UK but who process personal information in relation to the offering of goods or services to individuals in the UK, or to monitor their behavior will be subject to the UK GDPR—the requirements of which are (at this time) largely aligned with those under the EU GDPR. Further, on August 11, 2020, the UK Information Commissioner's Office (ICO) published its proposed draft International Transfer Risk Assessment and tool (TRA) which is the UK equivalent of the EDPB Recommendations and provides for general advice on how to satisfy the *Schrems II* requirement to carry out a legal assessment for transfers of personal data subject to the UK GDPR. It is expected that the final version of the TRA will be published in early 2022. The UK's ICO has also recently published: (i) its International Data Transfer Agreement to replace the old Standard Contractual Clauses for transfers to outside the UK; and (ii) a "UK addendum" to the new EU Standard Contractual Clauses which amends the relevant provisions of such clauses to work in a UK context.

As a company, we are in the process of implementing a GDPR compliance program. This is necessary to ensure we can initiate GDPR-compliant clinical trials in the EU. Failure to do so would mean we either cannot initiate GDPR-compliant clinical trials in the EU or we may face regulatory investigations, significant fines and penalties, reputational damage or be required to change our business practices, all of which could adversely affect our business, financial condition and results of operations.

Some countries also are considering or have passed legislation requiring local storage and processing of data, or similar requirements, which could increase the cost and complexity for conducting preclinical testing and clinical trials or delivering our future products, if any. Additionally, other countries (e.g., Australia and Japan) have adopted certain legal requirements for cross-border transfers of personal information. These obligations may be interpreted and applied in a manner that is inconsistent from one jurisdiction to another and may conflict with other requirements or our practices.

It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices and our efforts to comply with the evolving data protection rules may be unsuccessful. In addition to the possibility of fines, lawsuits, regulatory investigations, public censure, other claims and penalties, and significant costs for remediation and damage to our reputation, we could be materially and adversely affected if legislation or regulations are expanded to require changes in our data processing practices and policies or if governing jurisdictions interpret or implement their legislation or regulations in ways that negatively impact our business. 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 for ensuring compliance with the new data protection rules. If we or our third-party vendors, collaborators, contractors and consultants fail to comply with any such laws or regulations, we may face regulatory investigations, significant fines and penalties, reputational damage or be required to change our business practices, all of which could adversely affect our business, financial condition and results of operations. Any inability to adequately address data privacy or security-related concerns, even if unfounded, or to comply with applicable laws, regulations, standards and other obligations relating to data privacy and security, could result in additional cost and liability to us, harm our reputation and brand, damage our relationships with regulators and customers and have a material and adverse impact on our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

U.S. federal income tax reform and changes in other tax laws could adversely affect us.

In December 2017, U.S. federal tax legislation commonly referred to as the TCJA was signed into law, significantly reforming the Internal Revenue Code of 1986, as amended (Code). The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of business interest, allows for the expensing of capital expenditures, puts into effect the migration from a "worldwide" system of taxation to a partial "territorial" system, and modifies or repeals many business deductions and credits.

In March 2020, U.S. federal tax legislation named the CARES Act, was signed into law. Such legislation modified the TCJA by, among other things, eliminating the limitation on the deduction of NOLs to 80% of current year taxable income for tax years beginning before January 1, 2021, and increasing the amount of interest expense that may be deducted from 30% to 50% of adjusted taxable income for tax years beginning in 2019 or 2020.

The TCJA is a far-reaching and complex revision to the U.S. federal income tax laws with disparate and, in some cases, countervailing impacts on different categories of taxpayers and industries. The long-term impact of the TCJA, as modified by the CARES Act, on the overall economy, the industries in which we operate and our and our partners' businesses still cannot be reliably predicted. There can be no assurance that the TCJA, as modified by the CARES Act, will not negatively impact our future operating results. The estimated impact of the TCJA, as modified by the CARES Act, is based on our management's current knowledge and assumptions, following consultation with our tax advisors. Because of our valuation allowance in the United States, ongoing tax effects of the TCJA, as modified by the CARES Act, are not expected to materially change our effective tax rate in future periods.

In addition, new legislation or regulations that could affect our tax burden could be enacted by any governmental authority. We cannot predict the timing or extent of such tax-related developments that could negatively impact our financial results. Additionally, we use our best judgment in attempting to quantify and reserve for these tax obligations. However, a challenge by a taxing authority, our ability to utilize tax benefits such as carryforwards or tax credits, or a deviation from other tax-related assumptions could have a material adverse effect on our business, results of operations, or financial condition.

Our ability to utilize our net operating loss carryforwards may be subject to limitations.

We have incurred substantial losses during our history, do not expect to become profitable in the near future and may never achieve profitability. As of November 30, 2021, we had federal and state net operating loss (NOL) carryforwards of approximately $116.4 million and $192.1 million, respectively. To the extent we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, subject to the restrictions and exceptions described below. Federal NOLs generated in tax years beginning on or before December 31, 2017 may be carried forward 20 tax years and expire on various dates beginning in 2029. Under the TCJA, as modified by the CARES Act, NOLs arising in tax years beginning on or before December 31, 2017 may be carried back two tax years, NOLs arising in tax years beginning after December 31, 2017 and before January 1, 2021 may be carried back five tax years and NOLs arising in tax years beginning after December 31, 2020 may not be carried back. In 2020, we filed a refund claim of $15.7 million to carryback our NOLs generated in the fiscal year ended November 30, 2018, and we filed a refund claim to carryback our NOLs generated in the fiscal year ended November 30, 2019 to recover an additional $3.9 million of income tax. NOLs arising in tax years beginning after December 31, 2017 and before January 1, 2021 may be carried forward indefinitely but are limited to 80% of our taxable income in tax years beginning after December 31, 2020. State NOLs can be carried forward 20 years and begin expiring in 2029.

Under Sections 382 and 383 of the Code, if a corporation undergoes an “ownership change” (generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period), the corporation’s ability to use its pre-change NOLs and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. We have identified two ownership changes since our inception that have triggered a limitation on pre-change NOLs under Section 382. A majority of our pre-change NOLs remain available within the carryforward period provided by the Code, subject to availability of taxable income. We may have experienced additional ownership changes that have not yet been identified that could result in the expiration of our NOL and credit carryforwards before utilization and we may experience subsequent shifts in our stock ownership, some of which are outside our control. As a result, if we earn net taxable income, our ability to use our pre-change NOLs to offset U.S. federal taxable income may be subject to limitations that potentially could result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Future acquisitions, joint ventures, spin outs or strategic alliances or transactions could disrupt our business and harm our financial condition and results of operations.

We may acquire additional businesses or drugs, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new drugs resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot be certain that, following any such acquisition, we will achieve the expected synergies to justify the transaction. The risks we face in connection with acquisitions include:

- diversion of management time and focus from operating our business to addressing acquisition integration challenges;
- coordination of research and development efforts;
- retention of key employees from the acquired company;
- changes in relationships with strategic partners as a result of product acquisitions or strategic positioning resulting from the acquisition;
- cultural challenges associated with integrating employees from the acquired company into our organization;
- the need to implement or improve controls, procedures and policies at a business that prior to the acquisition may have lacked sufficiently effective controls, procedures and policies;
- liability for activities of the acquired company before the acquisition, including intellectual property infringement claims, violation of laws, commercial disputes, tax liabilities and other known liabilities;
- unanticipated write-offs or charges; and

- litigation or other claims in connection with the acquired company, including claims from terminated employees, customers, former stockholders or other third parties.

Our failure to address these risks or other problems encountered in connection with our past or future acquisitions or strategic alliances could cause us to fail to realize the anticipated benefits of these transactions, or cause us to incur unanticipated liabilities and harm the business generally. There also is a risk that future acquisitions will result in our incurring debt, contingent liabilities, amortization expenses or incremental operating expenses, any of which could harm our financial condition or results of operations. Additionally, we may not realize the expected value of out-licensing, joint ventures, spin outs or other strategic transactions.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, or other remedial measures and legal expenses, any of which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the Foreign Corrupt Practices Act (FCPA), the UK Bribery Act 2010 (Bribery Act) and other anticorruption laws that apply in countries where we do business and may do business in the future. The FCPA, the Bribery Act and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential FCPA or Bribery Act violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the FCPA, the Bribery Act or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We also are subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United States, UK and authorities in the EU, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, which we collectively refer to as Trade Control Laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA, the Bribery Act, or other legal requirements including Trade Control Laws. If we are not in compliance with the FCPA, the Bribery Act, and other anti-corruption laws or Trade Control Laws, we may be subject to criminal and civil penalties, legal expenses, and disgorgement and other sanctions and remedial measures, which could have an adverse impact on our business, financial condition, results of operations and liquidity. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. Likewise, any investigation of any potential violations of the FCPA, the Bribery Act, other anti-corruption laws or Trade Control Laws by U.S., UK or other authorities also could have an adverse impact on our reputation, our business, results of operations and financial condition.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could significantly harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may produce hazardous waste products. Although we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

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

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. Similarly, the volatility associated with the COVID-19 pandemic has caused significant instability and disruptions in the capital and credit markets and, in recent months, the global economy has been impacted by increasing interest rates and inflation. 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, global sanctions imposed in response thereto, or an energy crisis. 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. We cannot anticipate all of the ways in which the foregoing, and the current economic climate and financial market conditions 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.

Our current operations are in the San Francisco Bay Area, and we or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters as to which our business continuity and disaster recovery plans may not be adequate to protect us.

Our current operations are located in our facilities in San Francisco, California. Any unplanned event, such as earthquake, flood, fire, explosion, extreme weather condition, medical epidemic, power shortage, telecommunication failure or other natural or man-made accident or incident that result in our being unable to fully utilize our facilities, or the manufacturing facilities of our third-party contract manufacturers, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our drug candidates or interruption of our business operations, and have a material adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure such as our research facilities or the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our third-party contract manufacturers, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Our Common Stock

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

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

- variations in the level of expense related to the ongoing development of our drug candidates, DELigase platform, DeTIL or future development programs;
- results of preclinical and clinical trials, or the addition or termination of clinical trials or funding support by us or by existing or future collaborators or licensing partners;
- our execution of any additional collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under existing or future arrangements or the termination or modification of any such existing or future arrangements;
- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- additions and departures of key personnel;

- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- if any of our drug candidates receives regulatory approval, the terms of such approval and market acceptance and demand for such drug candidates;
- regulatory developments affecting our drug candidates or those of our competitors; and
- changes in general market and economic conditions, including increasing interest rates and inflation.

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

Our stock price may be volatile and you could lose all or part of your investment.

The trading price of our common stock may be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. As a result of this volatility, investors may not be able to sell their common stock at or above the purchase price. The market price for our common stock may be influenced by many factors, including the other risks described in this section and the following:

- results of preclinical studies and clinical trials of our drug candidates, or those of our competitors or our existing or future collaborators;
- regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to our drug candidates;
- the success of competitive products or technologies;
- introductions and announcements of new products by us, our collaboration partners, or our competitors, and the timing of these introductions or announcements;
- actions taken by regulatory agencies with respect to our drug candidates, clinical studies, manufacturing process or sales and marketing terms;
- actual or anticipated variations in our financial results or in those of companies that are perceived to be similar to us;
- the success of our efforts to acquire or in-license additional technologies, products or drug candidates;
- developments concerning our current or future collaborations, including but not limited to those with our sources of manufacturing supply and our commercialization partners;
- market conditions in the pharmaceutical and biotechnology sectors;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our drug candidates and products;
- our ability or inability to raise additional capital and the terms on which we raise it;
- the recruitment or departure of key personnel;
- changes in the structure of healthcare payment systems;
- actual or anticipated changes in earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may provide to the market;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- announcement and expectation of additional financing efforts;
- speculation in the press or investment community;

- trading volume of our common stock;
- sales of our common stock by us or our stockholders;
- the concentrated ownership of our common stock;
- changes in accounting principles;
- terrorist acts, acts of war or periods of widespread civil unrest, including the increasingly volatile global economic conditions resulting from the conflict in Ukraine;
- effects of public health crises, pandemics and epidemics, such as COVID-19;
- natural disasters and other calamities; and
- general economic, industry and market conditions, including increasing interest rates and inflation.

In addition, the stock market in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme price and volume fluctuations that often have been unrelated or disproportionate to the operating performance of the issuer. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and adverse impact on the market price of our common stock.

A sale of a substantial number of shares of our common stock may cause the price of our common stock to decline.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly.

We cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common stock. However, future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options, or the perception that such sales may occur, could adversely affect the market price of our common stock.

We also expect that significant additional capital may be needed in the future to continue our planned operations. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to 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.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock is and will be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not have any control over the analysts or the content and opinions included in their reports. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our preclinical studies and clinical trials and results of operations fail to meet the expectations of analysts, our stock price would likely decline. If one or more of such analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause a decline in our stock price or trading volume.

The future sale and issuance of equity or of debt securities that are convertible into equity will dilute our share capital.

We may choose to raise additional capital in the future, depending on market conditions, strategic considerations and operational requirements. For example, in March 2021, we sold an additional 5,175,000 shares of our common stock in a follow-on public offering. In addition, we currently have on file with the SEC a shelf registration statement on Form S-3 which allows us to offer and sell registered common stock, preferred stock, debt securities, warrants, subscriptions rights and or units from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. In August 2021, we entered into an Equity Distribution Agreement with Piper Sandler & Co. (Piper Sandler) pursuant to which, from time to time, we may offer and sell through Piper Sandler up to $150.0 million of the common stock registered under the shelf registration statement pursuant to one or more "at the market" offerings. In June 2022, we issued and sold 2,000,000 shares of common stock under the Equity Distribution Agreement to Piper Sandler for net proceeds of approximately $19.3 million, after deducting offering commissions and expenses paid by us. As of August 31, 2022, we had $130.0 million of common stock remaining available for sale pursuant to the Equity Distribution Agreement. Sales of our common stock under the Equity Distribution Agreement with Piper Sandler 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. In addition, in July 2022, we entered into separate Securities Purchase Agreements with certain purchasers to issue and sell pre-funded warrants to purchase an aggregate of 6,814,920 shares of our common stock in registered direct offerings for gross proceeds to us of $95.0 million before deducting offering expenses. Such pre-funded warrants are immediately exercisable, have an exercise price of $0.001 and may be exercised at any time after the date of issuance. To the extent additional capital is raised through the sale and issuance of shares or other securities convertible into shares, the ownership interest of our stockholders will be diluted. Future issuances of our common stock or other equity securities, or the perception that such sales may occur, could adversely affect the trading price of our common stock and impair our ability to raise capital through future offerings of shares or equity securities. No prediction can be made as to the effect, if any, that future sales of common stock or the availability of common stock for future sales will have on the trading price of our common stock.

We will not receive a significant amount, or potentially any, additional funds upon the exercise of our pre-funded warrants; however, any exercise would increase the number of shares eligible for future resale in the public market and result in substantial dilution to our stockholders.

As of August 31, 2022, we have issued pre-funded warrants to purchase a total of 6,814,920 shares of our common stock, of which 6,814,920 are outstanding. Each pre-funded warrant is exercisable for $0.001 per share of common stock underlying such pre-funded warrant, which may be paid by way of a cashless exercise, meaning that the holder may not pay a cash purchase price upon exercise, but instead would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. Accordingly, we will not receive a significant amount, or potentially any, additional funds upon the exercise of the pre-funded warrants. To the extent such pre-funded warrants are exercised, additional shares of common stock will be issued for nominal or no additional consideration, which will result in substantial dilution to the then existing holders of our common stock and will increase the number of shares eligible for resale in the public market. Sales of substantial numbers of such shares in the public market could adversely affect the market price of the common stock, causing our stock price to decline.

There is no public market for our pre-funded warrants.

There is no public trading market for our pre-funded warrants issued in July 2022, and we do not expect a market to develop. In addition, we do not intend to apply to list the pre-funded warrants on any securities exchange or nationally recognized trading system, including the Nasdaq Global Market (Nasdaq). Without an active market, the liquidity of the pre-funded warrants will be limited, and the value of the pre-funded warrants may be adversely impacted.

Additionally, each holder of pre-funded warrants will not be entitled to exercise any portion of any pre-funded warrant, which, upon giving effect to such exercise, would cause (i) the aggregate number of shares of our common stock beneficially owned by the holder (together with its affiliates) to exceed 9.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, or (ii) the combined voting power of our securities beneficially owned by the holder (together with its affiliates) to exceed 9.99% of the combined voting power of all of our securities then outstanding immediately after giving effect to the exercise. 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 us.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Our restated certificate of incorporation and our restated bylaws contain provisions that could delay or prevent a change in control of our company. These provisions also could make it difficult for stockholders to elect directors who are not nominated by current members of our board of directors or to take other corporate actions, including effecting changes in our management. These provisions:

- establish a classified board of directors so that not all members of our board are elected at one time;

- permit only our board of directors to establish the number of directors and fill vacancies on our board;
- provide that directors may be removed only "for cause" and only with the approval of two-thirds of our stockholders;
- require super-majority voting to amend some provisions in our restated certificate of incorporation and restated bylaws, unless such amendments are approved by two-thirds of our board of directors, in which case stockholders can approve by a simple majority;
- authorize the issuance of "blank check" preferred stock that our board could use to implement a stockholder rights plan;
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting; and
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings.

In addition, Section 203 of the Delaware General Corporation Law (DGCL) may discourage, delay or prevent a change in control of our company. Section 203 imposes certain restrictions on mergers, business combinations and other transactions between us and holders of 15% or more of our common stock.

Our restated certificate of incorporation and our restated bylaws contain exclusive forum provisions for certain claims, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our restated certificate of incorporation, to the fullest extent permitted by law, provides that the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the DGCL, our restated certificate of incorporation, or our restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine.

Moreover, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all claims brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder and our restated bylaws 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 (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. Section 27 of the Exchange Act creates exclusive federal jurisdiction over all claims brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder and neither the exclusive forum provision nor the Federal Forum Provision applies to suits brought to enforce any duty or liability created by the Exchange Act. Accordingly, actions by our stockholders to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder must be brought in federal court. Our stockholders will not be deemed to have waived our compliance with the federal securities laws and the regulations promulgated thereunder.

Any person or entity purchasing or otherwise acquiring or holding any interest in any of our securities shall be deemed to have notice of and consented to our exclusive forum provisions, including the Federal Forum Provision. These provisions may limit our stockholders' ability to bring a claim in a judicial forum they find favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers, and other employees. Alternatively, if a court were to find the choice of forum provision contained in our restated certificate of incorporation and/or restated 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, operating results and financial condition.

We will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we incur and, particularly now that we no longer are an emerging growth company, will further incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of Nasdaq and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Moreover, since we ceased to be an "emerging growth company" on November 30, 2021, we may no longer take advantage of certain exemptions from various reporting requirements that are applicable to public companies. This increase in reporting requirements will further increase our compliance burden.

Our management and other personnel are required to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements also could make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers. Moreover, these rules and regulations often are subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

If we fail to maintain effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock.

Pursuant to the rules and regulations of the SEC, we are required to furnish a report by our management on, among other things, our internal control over financial reporting. To achieve compliance with these rules and regulations, we engage in a process to document and evaluate our internal control over financial reporting, which is both costly and time consuming. Effective internal control over financial reporting is necessary for us to provide reliable financial reporting and, together with adequate disclosure controls and procedures, are designed to prevent material misstatements due to fraud or error. Any failure to design new or improved internal controls necessary to address risks of material misstatement in our interim or annual financial statements, or difficulties encountered in their implementation or operation, could cause us to fail to meet our reporting obligations. Ineffective internal control over financial reporting could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.

The reporting on our assessment of the effectiveness of our internal control over financial reporting needs to include disclosure of any material weaknesses identified in our internal control over financial reporting, as well as a statement that our independent registered public accounting firm has audited the effectiveness of our internal control over financial reporting. While we will qualify as a non-accelerated filer under SEC rules for fiscal year 2023 and therefore are not required to obtain such an audit for fiscal year 2023, in the event that we qualify as a large accelerated filer or accelerated filer under SEC rules in future years, our independent registered public accounting firm will be required to audit the effectiveness of our internal control over financial reporting, which will require increased costs, expenses, and management resources. Undetected material weaknesses in our internal control over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation. We are also required to disclose changes made in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, internal control over financial reporting on a quarterly basis. To comply with the requirements of being a public company, we have undertaken, and may need to further undertake in the future, various actions, such as implementing new internal controls and procedures and hiring additional accounting staff.

As discussed in Part I, Item 4 of this Quarterly Report on Form 10-Q, we have identified material weaknesses in our internal control over financial reporting related to controls over segregation of duties in our journal entry and account reconciliation processes, and certain information technology general controls. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis. As a result of the identified material weaknesses, our management concluded that our internal control over financial reporting was not effective as of November 30, 2021, which was previously reported in Part II, Item 9A of our Annual Report on Form 10-K for the fiscal year ended November 30, 2021. As of August 31, 2022, these material weaknesses have not been remediated. The material weaknesses identified in Part I, Item 4 of this Quarterly Report on Form 10-Q did not result in any misstatement of our financial statements. We have designed and have begun implementing a remediation plan for these material weaknesses. However, our remediation efforts may be inadequate, or we may in the future discover material weaknesses in other areas of our internal control over financial reporting that require remediation.

We cannot assure you that the measures we have taken to date, and actions we may take in the future, will be sufficient to remediate the control deficiencies that led to the material weaknesses in our internal control over financial reporting or that they will prevent or avoid potential future material weaknesses. Moreover, our current controls and any new controls that we develop may become inadequate because of changes in conditions in our business. Further, material weaknesses in our disclosure controls and procedures and internal control over financial reporting may be discovered in the future. Any failure to develop or maintain effective internal control over financial reporting or any difficulties encountered in their implementation or improvement could harm our operating results or cause us to fail to meet our reporting obligations and may result in a restatement of our financial statements for prior periods, which could cause the price of our common stock to decline. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq.

We are a "smaller reporting company" and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

Beginning with our Quarterly Report on Form 10-Q for the fiscal period ended May 31, 2022, we requalified as a "smaller reporting company," meaning that the market value of our stock held by non-affiliates is less than $560.0 million as of May 31, 2022, and our annual revenue is less than $100.0 million during the most recently completed fiscal year. We will 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 as of the prior May 31 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 of the prior May 31. As a smaller reporting company, we may take advantage of many of the same exemptions from disclosure requirements as an emerging growth company, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. 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.

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. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

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

The market price of our common stock may 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.

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

Use of Proceeds

On July 23, 2020, our registration statement on Form S-1, as amended (File No. 333-239651), was declared effective by the SEC in connection with the IPO of our common stock.

There has been no material change in the planned use of proceeds from our IPO as described in the prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act on July 24, 2020.

Unregistered Sales of Equity Securities

None.

Purchases of Equity Securities by Issuers and Affiliated Purchasers

None.

Item 3. Defaults Upon Senior Securities

None.

Item 4. Mine Safety Disclosures

None.

Item 5. Other Information

None.

Item 6. Exhibits

Exhibit Number	Description	Incorporated by Reference				Filed or Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
4.1	Form of Pre-funded Warrant	8-K	001-39398	4.1	July 8, 2022	
10.1	Form of Securities Purchase Agreement	8-K	001-39398	10.1	July 8, 2022	
10.2	First Amendment to Collaboration, Option and License Agreement, dated August 13, 2019, by and between the Registrant and Gilead Sciences, Inc.					X
10.3*	Second Amendment to Collaboration, Option and License Agreement, dated September 9, 2022, by and between the Registrant and Gilead Sciences, Inc.					X
10.4†	Second Amendment to Collaboration and License Agreement, dated December 16, 2021, by and between the Registrant and Genzyme Corporation					X
10.5†	Third Amendment to Collaboration and License Agreement, dated July 7, 2022, by and between the Registrant and Genzyme Corporation					X
10.6*†	Fourth Amendment to Collaboration and License Agreement, dated August 11, 2022, by and between the Registrant and Genzyme Corporation					X
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
32.1‡	Certification of Principal Executive Officer and Principal Financial and Accounting Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
101.INS	Inline XBRL Instance Document - the Instance Document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					X
104	Cover Page Interactive Data File (formatted as Inline XBRL and included in exhibit 101)					X

* *Registrant has omitted certain schedules pursuant to Item 601(a)(5) of Regulation S-K promulgated by the SEC.*

† *Registrant has omitted portions of the exhibit as permitted under Item 601(b)(10) of Regulation S-K.*

‡ *The certifications furnished in Exhibit 32.1 hereto are deemed to accompany this Quarterly Report on Form 10-Q and are not deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liability of that section, nor shall they be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.*

SIGNATURES

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

NURIX THERAPEUTICS, INC.

Date: October 6, 2022

By: /s/ Arthur T. Sands

Arthur T. Sands, M.D., Ph.D.
President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: October 6, 2022

By: /s/ Hans van Houte

Hans van Houte
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 10.2

FIRST AMENDMENT TO COLLABORATION, OPTION AND LICENSE AGREEMENT

This First Amendment to Collaboration, Option and License Agreement (this "***First Amendment***"), dated August 13, 2019 (the "***First Amendment Effective Date***"), is by and between Nurix Therapeutics, Inc., a Delaware corporation ("***Nurix***") and Gilead Sciences, Inc., a Delaware corporation ("***Gilead***").

RECITALS

WHEREAS, Nurix and Gilead entered into that certain Collaboration, Option and License Agreement, dated as of June 10, 2019 (the "***Collaboration Agreement***," and as amended by this First Amendment, the "***Agreement***"); and

WHEREAS, Nurix and Gilead wish to amend the Collaboration Agreement to clarify certain provisions thereunder, all in accordance with the terms set forth in this First Amendment.

NOW THEREFORE, in consideration of the mutual covenants and obligations set forth herein, Nurix and Gilead hereby agree to amend the Collaboration Agreement as follows:

AGREEMENT

1. **Definitions**. All capitalized terms not otherwise defined herein shall have the respective meanings assigned to them in the Collaboration Agreement.

2. **Ownership**. Section 12.5 of the Collaboration Agreement is hereby deleted in its entirety and replaced with the following:

12.5 Ownership.

12.5.1 Background and Sole IP. As between the Parties, each Party will retain ownership of all Patents, Know-How and other intellectual property rights that are Controlled by such Party prior to the Effective Date or are otherwise developed by such Party outside of this Agreement (with respect to such Party, its "Bac**kground IP**"). As between the Parties, and subject to the terms and conditions of this Section 12.5.1 (Background and Sole IP), all Inventions made or created solely by a Party's or any of its Affiliates' employees, independent contractors or consultants, in the course of conducting activities under this Agreement, together with all intellectual property rights therein, will be owned by such Party ("**Sole IP**"). Any Patent or Know-How covering any derivative or modification of or to a Gilead Target Binder, which derivative or modification (a) was developed by or on behalf of a Party or its Affiliates or jointly by or on behalf of the Parties or their Affiliates under this Agreement and (b) is designed to attach such Gilead Target Binder to a Linker, will be deemed Gilead Background IP (such Patent or Know-How, "**Gilead Target Binder IP**"). Nurix hereby assigns to Gilead, and will assign to Gilead, all of Nurix's rights, title and interests in and to any and all Gilead Target Binder IP. In addition, Nurix will promptly disclose to Gilead all Gilead Target Binder IP, and will perform all actions reasonably requested by Gilead to permit and assist Gilead in evidencing, perfecting, obtaining,

maintaining, defending and enforcing Gilead's rights in Gilead Target Binder IP, including executing all relevant documents (including written assignments to Gilead).

12.5.2 Joint IP. All Inventions made or created jointly by each Party's (or any of its Affiliates') employees, independent contractors or consultants, in the course of conducting activities under this Agreement, together with all Patents therein, will be jointly owned by the Parties ("**Joint IP**"). For clarity, any Patent or Know-How covering any compound (including any Degrader Compound) identified, synthesized or Researched under a Research Program, where the Target Binder incorporated in such compound (including Degrader Compound) is covered by any Patent or Know-How Controlled by Gilead or its Affiliates and was contributed by Gilead or its Affiliates, and the Linker incorporated in such compound (including Degrader Compound) is Controlled and was contributed by Nurix or one of its Affiliates, will be deemed Joint IP ("**Combined Degrader Compound IP**"). Subject to the terms and conditions of this Agreement (including this Article 12), Joint IP will be owned jointly by Gilead and Nurix on the basis of an equal, undivided interest without a duty to account to the other Party and will be deemed to be Controlled by each Party, and each Party will have the right to use such Joint IP, or license such Joint IP to its Affiliates or any Third Party, or sell or otherwise transfer its interest in such Joint IP to its Affiliates or a Third Party, in each case without the consent of the other Party. Notwithstanding the immediately preceding sentence, but subject to the remaining terms of this Agreement (including the remaining terms of this Article 12), each Party will only have the right to use Combined Degrader Compound IP, or license such Combined Degrader Compound IP to its Affiliates or any Third Party, or sell or otherwise transfer its interest in such Combined Degrader Compound IP to its Affiliates or a Third Party, in each case, without the consent of the other Party, if and so long as such use, sale, license or transfer is limited to Research activities. If a Party wishes to use any Combined Degrader Compound IP in any Development or Commercialization activities on behalf of itself, its Affiliates or any Third Party, such Party shall provide written notice to the other Party, and the Parties will negotiate with one another in good faith for one hundred and eighty (180) days to agree upon the royalties to be paid to the other Party for use of such Combined Degrader Compound IP in such Development or Commercialization activities. In the event that the Parties are unable to reach agreement on such royalties within the one hundred and eighty (180) day period as described above, then either Party may submit such matter to baseball arbitration for resolution in accordance with Section 17.6.3 (Baseball Arbitration).

12.5.3 Inventorship. All determinations of inventorship under this Agreement will be made in accordance with U.S. patent law.

3. General. Except as expressly set fo1th herein, the Collaboration Agreement shall continue in full force and effect and, as modified or amended, is hereby ratified, confirmed and approved.

Notwithstanding the foregoing, in the event of any conflict between the terms of this First Amendment and the terms of the Collaboration Agreement, the terms of this First Amendment shall control. No provision of this First Amendment may be modified or amended except expressly in a writing signed by both Parties nor shall any terms be waived except expressly in a writing signed by the Party charged therewith. This First Amendment shall be governed in accordance with the laws of the State of California, without giving effect to any choice of law rules. This First Amendment may be executed in counterparts with the same effect as if both Parties had signed the same document.

(*Remainder of Page Intentionally Left Blank; Signature Page Follows*)

IN WITNESS WHEREOF, and intending to be legally bound hereby, the Parties have entered into this First Amendment to be executed by their respective duly authorized officers as of the First Amendment Effective Date.

NURIX THERAPEUTICS, INC.	**GILEAD SCIENCES, INC.**
By: /s/ Pierre Beaurang_____	By: /s/ Muhieddine Makkouk_____
Name:Pierre Beaurang	Name:Muhieddine Makkouk
Title:Chief Business Officer	Title:VP, Alliance Management & Strategy

Exhibit 10.3

SECOND AMENDMENT TO COLLABORATION, OPTION AND LICENSE AGREEMENT

This Second Amendment to Collaboration, Option and License Agreement (this "**Second Amendment**"), dated September 9, 2022 (the "**Second Amendment Effective Date**"), is by and between Nurix Therapeutics, Inc., a Delaware corporation ("**Nurix**") and Gilead Sciences, Inc., a Delaware corporation ("**Gilead**").

RECITALS

WHEREAS, Gilead and Nurix are parties to that certain Collaboration, Option and License Agreement, dated June 10, 2019, as amended by that certain First Amendment dated August 13, 2019 (the "**Agreement**"); and

WHEREAS, the Parties wish to amend the Agreement to clarify certain provisions in Section 1 of Schedule 11.6, all in accordance with the terms set forth in this Second Amendment.

NOW, THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties agree as follows:

AGREEMENT

1. Definitions. All capitalized terms used herein shall have the respective meanings assigned to them in the Agreement.

2. Schedule 11.6. Schedule 11.6 to the Agreement is hereby deleted in its entirety and replaced with the Schedule 11.6 attached hereto.

3. General. Except as expressly set forth herein, the Agreement shall continue in full force and effect and, as modified or amended, is hereby ratified, confirmed and approved. Notwithstanding the foregoing, in the event of any conflict between the terms of this Second Amendment and the terms of the Agreement, the terms of this Second Amendment shall control. No provision of this Second Amendment may be modified or amended except expressly in a writing signed by both Parties nor shall any terms be waived except expressly in a writing signed by the Party charged therewith. This Second Amendment shall be governed in accordance with the laws of the State of California, without giving effect to any choice of law rules. This Second Amendment may be executed in counterparts with the same effect as if both Parties had signed the same document.

[*Signature Page Follows*]

IN WITNESS WHEREOF, the Parties, intending to be bound, have caused this Second Amendment to be duly executed and delivered by their respective authorized representatives as of the Second Amendment Effective Date.

GILEAD SCIENCES, INC.

By: /s/ Mary McGrath

Name: Mary McGrath

Title: Vice President, Research, SB&C

NURIX THERAPEUTICS, INC.

By: /s/ Christine Ring

Name: Christine Ring

Title: General Counsel

Schedule 11.6

Criteria for Pre-Clinical Milestone Events

Exhibit 10.4

CERTAIN INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [*], HAS BEEN OMITTED BECAUSE IT IS NOT MATERIAL AND IS THE TYPE OF INFORMATION THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.

SECOND AMENDMENT TO COLLABORATION AND LICENSE AGREEMENT

This Second Amendment to Collaboration and License Agreement (this "**Amendment**") is entered into as of December 16, 2021 (the "**Amendment Date**") by and between Genzyme Corporation, a Massachusetts corporation ("**Sanofi**"), and Nurix Therapeutics, Inc., a Delaware corporation ("**Nurix**"). Sanofi and Nurix are each referred to herein by name or, individually, as a "**Party**" or, collectively, as the "**Parties**."

Recitals

Whereas, the Parties entered into that certain Collaboration and License Agreement (as amended by the First Amendment, the "**Agreement**"), dated December 19, 2019, and that certain First Amendment to Collaboration and License Agreement, dated January 6, 2021 (the "**First Amendment**"); and

Whereas, the Parties wish to amend the Agreement to modify certain terms and conditions thereof as further described herein.

Now Therefore, in consideration of the foregoing premises and the mutual promises, covenants and conditions contained in this Amendment, in accordance with Section 18.5 of the Agreement, the Parties agree as follows:

1. Defined Terms. As used in this Amendment, capitalized terms, whether used in the singular or plural form, that are capitalized but not defined herein shall have the meanings ascribed to such terms in the Agreement.

2. Amendments.

(a) Section 2.2.3 of the Agreement is hereby deleted in its entirety and replaced with the following:

2.2.3 Collaboration Target Substitution Right. On a Collaboration Target-by-Collaboration Target basis, during the period of time beginning on the first day of the Collaboration Target Research Term for such Collaboration Target and [*] (such time period the "**Collaboration Target Substitution Period**"), Sanofi shall have the right, for any reason and at no cost to Sanofi, to substitute such Collaboration Target (a) for a Reserved Target upon delivery of written notice to Nurix's Alliance Manager prior to the expiration of the applicable Collaboration Target Substitution Period, or (b) subject to Section 2.4 (Proposed Targets), for an Available Target (collectively, the "**Collaboration Target Substitution Right**") (each such Collaboration Target that is replaced by a Reserved Target or Available Target thereafter a "**Replaced Collaboration Target**" and each such new Collaboration Target that is substituted for the Replaced Collaboration Target, a "**Substituted Collaboration Target**"), provided, however, that (x) there will in no event be more than five (5) Collaboration Targets in total

under this Agreement at any time during the Research Term, (y) at any given time during the Research Term, there will be no more than five (5) Research Programs with Collaboration Targets then ongoing, and (z) Sanofi shall only have the right to exercise its Collaboration Target Substitution Right [*] per Collaboration Target for [*], after which Sanofi shall no longer have the right to exercise its Collaboration Target Substitution Right.

(b) Section 2.10.1 of the Agreement is hereby deleted in its entirety and replaced with the following:

2.10.1 Target Exclusivity. Nurix will not conduct, and will cause its Affiliates to not conduct, by itself or themselves, or in collaboration with or on behalf of any Third Party, any Research, Development, Manufacture or Commercialization activities with respect to (a) any Collaboration Target for the period of time [*] applicable to such Collaboration Target, including such activities with respect to any compound Directed To such Collaboration Target alone or together with any other Target(s), (b) any Replaced Collaboration Target, any Collaboration Target terminated by Sanofi pursuant to ARTICLE 17 (Term and Termination), or any other Collaboration Target for which a License Term Extension does not occur within the License Extension Fee Timeframe, for a period of [*] after the date Sanofi has exercised its Collaboration Target Substitution Right with respect to any such Replaced Collaboration Target, the effective date of any such termination by Sanofi, or the last day of the License Extension Fee Timeframe (in each case as applicable), including such activities with respect to any compound Directed To such Target alone or together with any other Target(s), and (c) any Reserved Target during the Research Term, including such activities with respect to any compound Directed To such Target alone or together with any other Target(s) (each such time period a "**Target Exclusivity Period**"), in each case (a), (b) and (c) other than such Research activities expressly contemplated herein. Notwithstanding anything to the contrary in this Agreement, including the foregoing clause (b), if Sanofi exercises its Collaboration Target Substitution Right to replace [*], then the Target Exclusivity Period with respect to [*], as applicable, shall be a period of [*] after the date Sanofi has exercised its Collaboration Target Substitution Right with respect to such Target and not [*].

3. Miscellaneous.

(a) No Other Amendments. This Amendment shall be deemed to be a part of and incorporated into the Agreement. In the event of a conflict between this Amendment and the Agreement, this Amendment shall control. Except as expressly set forth in this Amendment, all of the terms and conditions of the Agreement shall remain unchanged and are ratified and confirmed in all respects and remain in full force and effect.

(b) Entire Agreement. This Amendment, together with the Agreement and any exhibits or attachments thereto, contains the entire agreement by the Parties with respect to the subject matter hereof, and any reference to the Agreement shall refer to the Agreement, as amended by this Amendment.

(c) Counterparts. This Amendment may be executed in counterparts with the same effect as if both Parties had signed the same document. All such counterparts will be deemed an original, will be construed together and will constitute one and the same instrument. Any such counterpart, to the extent delivered by Electronic Delivery, will be treated in all manner and respects as an original executed counterpart and will be considered to have the same binding legal effect as if

it were the original signed version thereof delivered in person. No Party will raise the use of Electronic Delivery to deliver a signature or the fact that any signature or agreement or instrument was transmitted or communicated through the use of Electronic Delivery as a defense to the formation of a contract, and each Party forever waives any such defense, except to the extent that such defense relates to lack of authenticity.

(d) Choice of Law. This Amendment and any Dispute arising from the performance or breach hereof will be governed by and interpreted in accordance with the laws of the State of New York, without giving effect to any choice of law rules.

[Signature Page Follows]

In Witness Whereof, and intending to be legally bound hereby, the Parties have caused this Amendment to be executed by their respective duly authorized representatives as of the Amendment Date.

NURIX THERAPEUTICS, INC.	**GENZYME CORPORATION**
By:/s/ Christine Ring	By: /s/ Monsif Bouaboula
Name: Christine Ring	Name: Monsif Bouaboula
Title: General Counsel	Title: Group Head

Exhibit 10.5

CERTAIN INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [*], HAS BEEN OMITTED BECAUSE IT IS NOT MATERIAL AND IS THE TYPE OF INFORMATION THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.

THIRD AMENDMENT TO COLLABORATION AND LICENSE AGREEMENT

This Third Amendment to Collaboration and License Agreement (this "**Amendment**") is entered into as of July 7, 2022 (the "**Amendment Date**") by and between Genzyme Corporation, a Massachusetts corporation ("**Sanofi**"), and Nurix Therapeutics, Inc., a Delaware corporation ("**Nurix**"). Sanofi and Nurix are each referred to herein by name or, individually, as a "**Party**" or, collectively, as the "**Parties**."

Recitals

WHEREAS the Parties entered into that certain Collaboration and License Agreement (as amended by the Amendments, the "**Agreement**"), dated December 19, 2019, that certain First Amendment to Collaboration and License Agreement, dated January 6, 2021 (the "**First Amendment**"), and that certain Second Amendment to Collaboration and License Agreement, dated December 16, 2021 (the "**Second Amendment**" and, together with the First Amendment, the "**Amendments**"); and

WHEREAS the Parties wish to amend the Agreement to modify certain terms and conditions thereof as further described herein.

Now Therefore, in consideration of the foregoing premises and the mutual promises, covenants and conditions contained in this Amendment, in accordance with Section 18.5 of the Agreement, the Parties agree as follows:

1. Defined Terms. As used in this Amendment, capitalized terms, whether used in the singular or plural form, that are capitalized but not defined herein shall have the meanings ascribed to such terms in the Agreement.

2. Amendments.

(a) Section 2.2.3 of the Agreement is hereby deleted in its entirety and replaced with the following:

2.2.3 Collaboration Target Substitution Right. On a Collaboration Target-by-Collaboration Target basis, during the period of time beginning on the first day of the Collaboration Target Research Term for such Collaboration Target and [*] (such time period the "**Collaboration Target Substitution Period**"), Sanofi shall have the right, for any reason and at no cost to Sanofi, to substitute such Collaboration Target (a) for a Reserved Target upon delivery of written notice to Nurix's Alliance Manager prior to the expiration of the applicable Collaboration Target Substitution Period, or (b) subject to Section 2.4 (Proposed Targets), for an Available Target (collectively, the "**Collaboration Target Substitution Right**") (each such Collaboration Target that is replaced by a Reserved Target or Available Target thereafter a "**Replaced Collaboration Target**" and each such new Collaboration Target that is substituted

for the Replaced Collaboration Target, a "**Substituted Collaboration Target**"), provided, however, that (x) there will in no event be more than five (5) Collaboration Targets in total under this Agreement at any time during the Research Term, (y) at any given time during the Research Term, there will be no more than five (5) Research Programs with Collaboration Targets then ongoing, and (z) Sanofi shall only have the right to exercise its Collaboration Target Substitution Right [*] per Collaboration Target for [*], after which Sanofi shall no longer have the right to exercise its Collaboration Target Substitution Right.

3. Miscellaneous.

(a) No Other Amendments. This Amendment shall be deemed to be a part of and incorporated into the Agreement. In the event of a conflict between this Amendment and the Agreement, this Amendment shall control. For clarity, except as expressly set forth in this Amendment, all of the terms and conditions of the Agreement, including without limitation, the terms of Section 1.44 (Collaboration Target Research Term) and Section 1.193 (Research Term), shall remain unchanged and are ratified and confirmed in all respects and remain in full force and effect.

(b) Entire Agreement. This Amendment, together with the Agreement and any exhibits or attachments thereto, contains the entire agreement by the Parties with respect to the subject matter hereof, and any reference to the Agreement shall refer to the Agreement, as amended by this Amendment.

(c) Counterparts. This Amendment may be executed in counterparts with the same effect as if both Parties had signed the same document. All such counterparts will be deemed an original, will be construed together and will constitute one and the same instrument. Any such counterpart, to the extent delivered by Electronic Delivery, will be treated in all manner and respects as an original executed counterpart and will be considered to have the same binding legal effect as if it were the original signed version thereof delivered in person. No Party will raise the use of Electronic Delivery to deliver a signature or the fact that any signature or agreement or instrument was transmitted or communicated through the use of Electronic Delivery as a defense to the formation of a contract, and each Party forever waives any such defense, except to the extent that such defense relates to lack of authenticity.

(d) Choice of Law. This Amendment and any Dispute arising from the performance or breach hereof will be governed by and interpreted in accordance with the laws of the State of New York, without giving effect to any choice of law rules.

[Signature Page Follows]

In Witness Whereof, and intending to be legally bound hereby, the Parties have caused this Amendment to be executed by their respective duly authorized representatives as of the Amendment Date.

NURIX THERAPEUTICS, INC.	**GENZYME CORPORATION**
By:/s/ Christine Ring	By: /s/ Monsif Bouaboula
Name: Christine Ring	Name: Monsif Bouaboula
Title: General Counsel	Title: Group Head

Exhibit 10.6

CERTAIN INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [*], HAS BEEN OMITTED BECAUSE IT IS NOT MATERIAL AND IS THE TYPE OF INFORMATION THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.

FOURTH AMENDMENT TO COLLABORATION AND LICENSE AGREEMENT

This Fourth Amendment to Collaboration and License Agreement (this "**Amendment**") is entered into as of August 11, 2022 (the "**Amendment Date**") by and between Genzyme Corporation, a Massachusetts corporation ("**Sanofi**"), and Nurix Therapeutics, Inc., a Delaware corporation ("**Nurix**"). Sanofi and Nurix are each referred to herein by name or, individually, as a "**Party**" or, collectively, as the "**Parties**."

Recitals

WHEREAS the Parties entered into that certain Collaboration and License Agreement (as amended by the Amendments, the "**Agreement**"), dated December 19, 2019, that certain First Amendment to Collaboration and License Agreement, dated January 6, 2021 (the "**First Amendment**"), that certain Second Amendment to Collaboration and License Agreement, dated December 16, 2021 (the "**Second Amendment**"), and that certain Third Amendment to Collaboration and License Agreement, dated July 7, 2022 (the "**Third Amendment**" and, together with the First Amendment and the Second Amendment, the "**Amendments**"); and

WHEREAS the Parties wish to amend the Agreement to modify the Research Plan for Collaboration Target [*] under Exhibit A under which Sanofi will conduct Research relating to [*], and to modify certain terms and conditions of the Agreement with respect to such Research as further described herein.

Now Therefore, in consideration of the foregoing premises and the mutual promises, covenants and conditions contained in this Amendment, in accordance with Section 18.5 of the Agreement, the Parties agree as follows:

1. Defined Terms. As used in this Amendment, capitalized terms, whether used in the singular or plural form, that are capitalized but not defined herein shall have the meanings ascribed to such terms in the Agreement.

2. Amendments.

(a) An amended Research Plan for the [*] is attached hereto as Exhibit A. Such Research Plan shall be deemed approved by the JRC as of the Amendment Date. For clarity:

(i) all pre-clinical research activities under such amended Research Plan, including those activities conducted by Sanofi or its Affiliates, shall be deemed to be Research under the Agreement and part of the Research Program for the [*];

(ii) nothing in this Amendment is intended to modify the Research Term, including with respect to such amended Research Plan for the [*];

(iii) in accordance with, and subject to the terms and conditions of, Section 2.1.1 (Research Programs; General) of the Agreement, each Party shall bear its own costs and expenses incurred by or on behalf of it or its respective Affiliates in the performance of such Party's respective Research activities under such amended Research Plan;

(iv) in accordance with, and subject to the terms and conditions of, Section 12.1.1 (Research License to Nurix), Nurix may use Collaboration [*] (defined below) in its activities under the Research Plan for the [*], including for purposes of [*] such Collaboration [*] into [*] that are Directed To such [*].

(b) Section 1.127 of the Agreement is hereby deleted in its entirety and replaced with the following:

1.127 "**Licensed Product**" means any pharmaceutical preparation in final form containing (a) a CTM (including any Development Candidate) that has relevant pharmacological activity and is Directed To a Collaboration Target, or (b) a Selected Target Binder or Collaboration [*] that is Directed To a Collaboration Target and itself has relevant pharmacological activity (each, a "**Standalone Target Binder**"), in each case that was identified (except for [*]), synthesized and Researched by or on behalf of Nurix or its Affiliates and/or, solely in the case of Collaboration [*], Sanofi or its Affiliates, in each case pursuant to a Research Plan, prior to the expiration of the applicable Collaboration Target Research Term (whether alone or as part of a Combination Product, and in all presentations and formulations including manner of delivery and dosage).

(c) Section 1.198 of the Agreement is hereby deleted in its entirety and replaced with the following:

1.198 "**Reverted Product**" means all CTMs, Target Binders, Standalone Target Binders and Development Candidates (and backups thereto) that are Directed To a Reverted Target, but in each case excluding any [*] and any CTMs comprising a [*]; *provided*, *however*, for clarity, if the [*] becomes a Reverted Target, then Reverted Products shall include all Collaboration [*] that are: (a) derived by [*] from Target Binders [*]; or (b) identified or developed by [*] using (i) [*] or (ii) [*].

(d) Section 1.212 of the Agreement is hereby deleted in its entirety and replaced with the following:

1.212 "**Sanofi M1 Criteria**" means, with respect to a CTM or Target Binder, the criteria that serve as a basis for Sanofi's determination in accordance with its standard internal policies and formal governance procedures to further commit resources to potentially achieve [*] for such CTM or Target Binder, which criteria include [*].

(e) A new Section 1.242 is hereby added to the Agreement which shall provide as follows:

1.242 "**Amended** [*] **Research Plan**" means the amended Research Plan for the [*], attached as Exhibit A to Amendment No. 3 to the Agreement, as such plan may be further amended from time to time in accordance with this Agreement.

(f) A new Section 1.243 is hereby added to the Agreement which shall provide as follows:

1.243 "**Collaboration** [*]" means each [*] that: (a) is [*]; (b) [*]; and (c) is identified and Researched under Part 2 ([*]) of the [*]. For clarity, each Collaboration [*] is a Target Binder.

(g) A new Section 1.244 is hereby added to the Agreement which shall provide as follows:

1.244 "**Modulate**" means, with regard to a particular Target, that the compound or product at issue activates, inhibits, agonizes, antagonizes, or otherwise regulates or adjusts such Target, and such activation, inhibition, agonizing, antagonizing, or other regulation or adjustment causes pharmacologically relevant activity with respect to such Target.

(h) A new Section 1.245 is hereby added to the Agreement which shall provide as follows:

1.245 "[*] **Sanofi Background IP**" means Background IP Controlled by Sanofi consisting solely of: (a) Patents covering inventions that (i) were conceived or reduced to practice on or before [*] for the [*] (even if such Patents were applied for or issued after such date), (ii) are [*] into a Collaboration [*] or [*] pursuant to Section 2.9.1 (Information Sharing), and (iii) [*], pursuant to Section 17.7.2 (Reversion); and (b) Know-How that (i) was in existence on or before [*] for the [*], (ii) is [*] under Part 2 ([*]) of the [*] and that [*] pursuant to Section 2.9.1 (Information Sharing), and (iii) [*] to Research, Develop, Manufacture, or Commercialize a Reverted Product that is Directed To the [*]. [*].

(i) Section 2.7.4 of the Agreement is hereby deleted in its entirety and replaced with the following:

2.7.4 Activities to be Performed by Sanofi. The Parties agree that Sanofi shall have the right to perform certain research activities under the Agreement, including [*]. If Sanofi performs any such [*] research activities, then Nurix shall transfer upon request by Sanofi and at no cost to Sanofi, adequate amounts of biological and CTM materials and Target Binder materials (including protocols, control compounds, and reagents for related assays) for such purposes, in each case as may be specified in the applicable Research Plan or otherwise mutually agreed by the Parties via the JRC as reflected in written minutes approved in accordance with Section 9.2.2 of the Agreement. Prior to Nurix transferring any such materials to Sanofi, the Parties shall enter into a material transfer agreement in substantially the form set forth on Exhibit F to the Correspondence (a "**Material Transfer Agreement**").

(j) For clarity, Section 2.9.1 (Information Sharing) shall apply to all Research conducted by Sanofi under Part 2 ([*]) of the Amended [*] Research Plan. For further clarity,

notwithstanding anything to the contrary in Section 2.9.2 (Development Candidate Data Package) or Section 2.9.3 (Nurix Key Data Report) of the Agreement, [*] results of Sanofi's activities with respect to the Research under Part 2 ([*]) of the [*], as assigned to Sanofi under the [*].

(k) Section 2.10.3 of the Agreement is hereby deleted in its entirety and replaced with the following:

2.10.3 Research Results. All Research Results generated by or on behalf of (i) Nurix or (ii) solely in the case of Research Results related to Collaboration [*], either Party, in each case, under this Agreement or any Ancillary Agreement will be deemed the Confidential Information of both Parties, provided, however, that, if Sanofi fails to make a License Extension Fee for a Collaboration Target in accordance with Section 11.4 (License Extension Fee) prior to the expiration of the License Extension Fee Timeframe for such Collaboration License, then upon the expiration of the Target Exclusivity Period for such Target, all Research Results related to such Target that are generated by or on behalf of (i) Nurix or (ii) solely in the case of [*], either Party, in each case, in the performance of the Collaboration will be deemed the Confidential Information of Nurix, to the extent such Research Results do not include any data, results or other information pertaining to any CTM comprising a [*], any [*] or other Sanofi Materials, or, in the case of the [*], any [*], in each case, which will be deemed the Confidential Information of Sanofi. For clarity: (a) this Section 2.10.3 (Research Results) shall not limit Sanofi's ability to exercise the license set forth in Section 17.7.2(c) (Reversion), in accordance with the terms and conditions thereof; and (b) Sanofi's ability to use and disclose such Nurix Confidential Information to Third Parties is governed by Article 14 (Confidentiality), including Sanofi's right to make disclosures as further described in Section 14.3.1(e)(ii) under customary confidentiality and non-use obligations, to the extent necessary or reasonably useful for Sanofi to exercise its rights under the license set forth in Section 17.7.2(c) (Reversion).

(l) Section 7.1 of the Agreement is hereby deleted in its entirety and replaced with the following:

7.1 Manufacturing. Subject to the terms and conditions of this Agreement, (a) Nurix, at its sole cost and expense, will Manufacture, itself or through Third Parties, Research supplies (other than GLP tox supplies) for the Parties' use of the respective CTMs, Target Binders and Development Candidates in the Field in the Territory under the Collaboration, provided that [*], provided, further, that Research supplies for Sanofi shall be limited to those specified in any Research Plan for Sanofi activities or otherwise as permitted under Section 2.7.4 (Activities to be Performed by Sanofi), and (b) Sanofi will have the sole and exclusive right to Manufacture (and will solely and exclusively control, at its discretion, the Manufacture of), itself or with or through its Affiliates, Sublicensees or other Third Parties, the GLP tox supplies, and supplies to support Development or Commercial activities for the respective Development Candidates, backups thereto and Licensed Products in the Field in the Territory. Subject to the Co-Development/Co-Commercialization Agreement and Profit/Loss Share Agreement (if executed), all such Manufacturing described in clause (b) will be at Sanofi's sole cost and expense. Notwithstanding the foregoing, Sanofi shall have the right, but not the obligation, to Manufacture, itself or through Third Parties, Research supplies of [*] to enable Sanofi's activities with respect to the Research of Collaboration [*], as assigned to Sanofi under the [*]. Upon request, Nurix shall provide Sanofi with [*] for Sanofi to be able to Manufacture such Research supplies, including, without limitation, [*] for the relevant

Collaboration [*].

(m) Notwithstanding anything in Article 8 (Nurix Options) to the contrary: (i) under Section 8.1 (Delivery of Profit/Loss Share Data Package to Nurix), if [*] is achieved for a Licensed Product that is a [*] (a "[*]") and/or a [*], then Sanofi will provide Nurix with a Profit/Loss Share Data Package for [*] Licensed Product Directed To the [*] that achieves [*]; and (ii) under Section 8.2 (Option Exercise), [*], Nurix may elect to exercise a Co-Development/Co-Promotion Option for [*], in each case, after receiving the Profit/Loss Share Data Package for the [*]. If (a) Nurix elects to exercise the Co-Development/Co-Promotion Option for [*] after receiving such Profit/Loss Share Data Package and (b) [*], then Sanofi will [*] for the [*]; provided that, for clarity, [*], which shall [*]. [*].

(n) Section 9.4.1 of the Agreement is hereby deleted in its entirety and replaced with the following:

9.4.1 JRC Decisions. Each Party will have one vote at the JRC. The JRC will endeavor to make decisions by consensus. In the absence of consensus, any dispute will be escalated to the Executive Officers, and if the Executive Officers are unable to resolve such dispute within [*] Business Days after such matter has been referred to them then (a) for matters relating to [*], Nurix shall have final decision-making ability; *provided that*, Sanofi shall have final decision-making ability for matters relating to [*], and (b) for all other matters and any matter overseen by the JRC, Sanofi shall have final decision-making ability. For clarity, Nurix shall not use its final decision-making ability to (i) [*]; (ii) [*] or (iii) [*].

(o) Exhibit B attached to this Amendment is hereby added to Schedule 1.188 (Research Milestone Event Criteria) to the Agreement, solely with respect to [*]. For clarity, with respect to Licensed Products other than [*], Schedule 1.188 shall remain unchanged.

(p) Clause (a) of Section 13.2.1 of the Agreement is hereby deleted in its entirety and replaced with the following:

(a) Before License Term Extension. Prior to the occurrence of a License Term Extension with respect to a Collaboration Target, [*] will be responsible for the Prosecution and Maintenance of Product Patents, including [*], at [*] sole cost and expense. Product Patents invented [*] will be Prosecuted and Maintained [*], Product Patents invented [*] will be Prosecuted and Maintained in [*], and Product Patents that are [*] will be Prosecuted and Maintained in [*], provided that [*].

(q) For clarity: (1) all Inventions made or created solely by Sanofi's or its Affiliates' employees, independent contractors or consultants in the course of conducting activities under Part 2 ([*]) of the [*] will be Foreground IP [*] in accordance with Section 13.1.1 (General); and (2) such Foreground IP (A) is licensed to Nurix in accordance with Section 12.1.1 (Research License to Nurix), including for purposes of the Research to be conducted by Nurix or its Affiliates under Part 1 of the [*], and (B) would be [*].

(r) Section 17.7.2 of the Agreement is hereby deleted in its entirety and replaced with the following:

17.7.2 Reversion.

(a) Sanofi hereby grants to Nurix (i) [*] license, under [*] to Develop, Manufacture and Commercialize all Reverted Products in the Field in each applicable country in the Territory, subject to Nurix's obligations under Section 2.10.1 (Target Exclusivity), and (ii) solely in the case of the [*], [*], subject to Nurix's obligations under Section 2.10.1 (Target Exclusivity). Nurix will only exercise its rights under the foregoing license in accordance with Section 12.2 (Expiration; License Term Extension), if Sanofi fails to make the License Extension Fee for the applicable Collaboration Target in accordance with Section 11.4 (License Extension Fee) prior to the expiration of the License Extension Fee Timeframe for such Collaboration License, and will only exercise its rights under the foregoing license with respect to Reverted Products in existence as of the expiration date of the applicable Collaboration License. For clarity, Sanofi shall retain the right to use [*] for [*], and all such other intellectual property rights, Patents or Know-How owned or Controlled by Sanofi for [*] other than with respect to a Reverted Product. Nurix shall have the right to terminate all or any portion of the rights granted to it under this 17.7.2 (Reversion), upon written notice to Sanofi. Subject to the previous sentence, Nurix shall pay to Sanofi royalties on Annual Net Sales (as such term is applied *mutatis mutandis* to Nurix and its Affiliates and sublicensees) of: (a) Reverted Products that [*] or, (b) solely with respect to [*], to the extent Covered by [*]. For clarity, with respect to [*], the license granted to Nurix in this Section 17.7.2 shall be [*].

(b) [*].

(c) Nurix hereby grants to Sanofi a [*] license, under the Research Results generated by Sanofi related to [*] that became the sole Confidential Information of Nurix upon the expiration of the Target Exclusivity Period for the [*] in accordance with Section 2.10.3 (Research Results) to use for [*].

(s) Section 13.2.4 of the Agreement is hereby deleted in its entirety and replaced with the following:

13.2.4 Cooperation via JPC. A Party that Prosecutes and Maintains any Patent in accordance with this Section 13.2 (Prosecution and Maintenance) (the "**Prosecuting Party**") will keep the other Party (the "**Non-Prosecuting Party**") reasonably informed of the status of such Patent via the JPC. The Non-Prosecuting Party will fully cooperate with the Prosecuting Party in connection with the Prosecution and Maintenance of such Patents described in Section 13.2.1 (Before License Term Extension) and Section 13.2.1(b) (After License Term Extension), including as set forth in Section 13.1.2 (Invention Assignments) above. With respect to Non-Product Patents, Sanofi will have an opportunity to comment through the JPC on the Prosecution and Maintenance of such Non-Product Patent solely to the extent [*]. Each Party through the JPC will promptly notify the other Party of any opposition by a Third Party or similar adverse proceeding by a Third Party with respect to a Product Patent or, to the extent described in the foregoing sentence, a Non-Product Patent, of which it becomes aware.

3. Miscellaneous.

(a) No Other Amendments. This Amendment shall be deemed to be a part of and incorporated into the Agreement. In the event of a conflict between this Amendment and the Agreement, this Amendment shall control. Except as expressly set forth in this Amendment, all of the terms and conditions of the Agreement, including without limitation rights and obligations with respect

to Patents and Know-How, shall remain unchanged and are ratified and confirmed in all respects and remain in full force and effect.

(b) Entire Agreement. This Amendment, together with the Agreement and any exhibits or attachments thereto, contains the entire agreement by the Parties with respect to the subject matter hereof, and any reference to the Agreement shall refer to the Agreement, as amended by this Amendment.

(c) Counterparts. This Amendment may be executed in counterparts with the same effect as if both Parties had signed the same document. All such counterparts will be deemed an original, will be construed together and will constitute one and the same instrument. Any such counterpart, to the extent delivered by Electronic Delivery, will be treated in all manner and respects as an original executed counterpart and will be considered to have the same binding legal effect as if it were the original signed version thereof delivered in person. No Party will raise the use of Electronic Delivery to deliver a signature or the fact that any signature or agreement or instrument was transmitted or communicated through the use of Electronic Delivery as a defense to the formation of a contract, and each Party forever waives any such defense, except to the extent that such defense relates to lack of authenticity.

(d) Choice of Law. This Amendment and any Dispute arising from the performance or breach hereof will be governed by and interpreted in accordance with the laws of the State of New York, without giving effect to any choice of law rules.

[Signature Page Follows]

In Witness Whereof, and intending to be legally bound hereby, the Parties have caused this Amendment to be executed by their respective duly authorized representatives as of the Amendment Date.

NURIX THERAPEUTICS, INC.	**GENZYME CORPORATION**
By: /s/ Christine Ring	By: /s/ Matthew J. LaMarche
Name: Christine Ring	Name: Matthew J. LaMarche
Title: General Counsel	Title: US Site Head, Integrated Drug Discover

Exhibit 31.1

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

I, Arthur T. Sands, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Nurix 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 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.

By: /s/ Arthur T. Sands
Arthur T. Sands, M.D., Ph.D.
President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: October 6, 2022

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL AND ACCOUNTING OFFICER PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Hans van Houte, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Nurix 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 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.

By: /s/ Hans van Houte
Hans van Houte
Chief Financial Officer
(Principal Financial and Accounting Officer)

Date: October 6, 2022

Exhibit 32.1

CERTIFICATIONS PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002
(18 U.S.C. SECTION 1350)

Each of the undersigned officers of Nurix Therapeutics, Inc. (the Company) certifies, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Quarterly Report on Form 10-Q of the Company for the quarter ended August 31, 2022 (the Quarterly Report), as filed with the Securities and Exchange Commission, 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 this Quarterly Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

By: /s/ Arthur T. Sands
Arthur T. Sands, M.D., Ph.D.
President, Chief Executive Officer and Director
(Principal Executive Officer)

By: /s/ Hans van Houte
Hans van Houte
Chief Financial Officer
(Principal Financial and Accounting Officer)

Date: October 6, 2022