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

FORM 10-Q

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

For the quarterly period ended September 30, 2024

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: 001-37766

INTELLIA THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**36-4785571**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
40 Erie Street, Suite 130, Cambridge, Massachusetts	**02139**
(Address of Principal Executive Offices)	**(Zip Code)**

857-285-6200
(Registrant's Telephone Number, Including Area Code)

Securities Registered Pursuant to Section 12(b) of the Act:

Title of each Class	Trade Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	NTLA	The Nasdaq Global Market

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 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 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 Act). Yes ☐ No ☒

The number of shares outstanding of the registrant's common stock as of November 1, 2024: 101,848,572 shares.

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PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

INTELLIA THERAPEUTICS, INC.
Condensed Consolidated Balance Sheets (unaudited)
(Amounts in thousands except share and per share data)

	September 30, 2024	December 31, 2023
ASSETS		
Current assets:		
Cash and cash equivalents	$ 120,495	$ 226,748
Marketable securities	537,619	685,475
Accounts receivable	8,854	36,456
Prepaid expenses and other current assets	43,934	49,651
Total current assets	710,902	998,330
Marketable securities - noncurrent	286,567	99,864
Property and equipment, net	28,763	32,760
Operating lease right-of-use assets	100,331	115,375
Equity method investment	-	11,765
Investments and other assets	46,788	42,883
Total assets	$ 1,173,351	$ 1,300,977
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 13,145	$ 7,452
Accrued expenses	51,206	67,017
Current portion of operating lease liability	19,177	18,599
Current portion of deferred revenue	22,155	22,140
Total current liabilities	105,683	115,208
Deferred revenue, net of current portion	22,607	38,853
Long-term operating lease liability	82,446	96,747
Total liabilities	210,736	250,808
Commitments and contingencies (Note 6)		
Stockholders' equity:		
Common stock, $0.0001 par value; 240,000,000 shares authorized at September 30, 2024 and December 31, 2023; 101,796,365 and 92,997,158 shares issued and outstanding at September 30, 2024 and December 31, 2023, respectively	10	9
Additional paid-in capital	3,007,810	2,710,797
Accumulated other comprehensive income (loss)	3,297	(2,258)
Accumulated deficit	(2,048,502)	(1,658,379)
Total stockholders' equity	962,615	1,050,169
Total liabilities and stockholders' equity	$ 1,173,351	$ 1,300,977

See notes to condensed consolidated financial statements.

INTELLIA THERAPEUTICS, INC.
Condensed Consolidated Statements of Operations and Comprehensive Loss (unaudited)
(Amounts in thousands except per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Collaboration revenue	$ 9,111	$ 11,992	$ 45,003	$ 38,192
Operating expenses:				
Research and development	123,380	113,696	349,434	326,088
General and administrative	30,501	29,403	93,385	87,503
Total operating expenses	153,881	143,099	442,819	413,591
Operating loss	(144,770)	(131,107)	(397,816)	(375,399)
Other income (expense), net:				
Interest income	12,122	12,740	37,176	37,373
Change in fair value of investments, net	(3,064)	-	(29,483)	-
Loss from equity method investment	-	(3,857)	-	(10,905)
Change in fair value of contingent consideration	-	-	-	(100)
Total other income, net	9,058	8,883	7,693	26,368
Net loss	$ (135,712)	$ (122,224)	$ (390,123)	$ (349,031)
Net loss per share, basic and diluted	$ (1.34)	$ (1.38)	$ (3.99)	$ (3.96)
Weighted average shares outstanding, basic and diluted	101,002	88,645	97,842	88,204
Other comprehensive income:				
Unrealized gain on marketable securities	4,452	142	3,423	1,649
Other comprehensive gain from equity method investment	-	154	-	2,240
Comprehensive loss	$ (131,260)	$ (121,928)	$ (386,700)	$ (345,142)

See notes to condensed consolidated financial statements.

INTELLIA THERAPEUTICS, INC.
Condensed Consolidated Statements of Stockholders' Equity (unaudited)
(Amounts in thousands except share data)

	Common Shares	Common Amount	Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2023	92,997,158	$ 9	$ 2,710,797	$ (2,258)	$ (1,658,379)	$ 1,050,169
Issuance of common stock through at-the-market offerings, net of issuance costs of $210	2,209,938	1	55,958	-	-	55,959
Exercise of stock options	110,734	-	1,958	-	-	1,958
Vesting of restricted stock units	1,015,543	-	-	-	-	-
Stock-based compensation	-	-	34,176	-	-	34,176
Other comprehensive income (loss) - unrealized loss on marketable securities	-	-	-	(821)	-	(821)
Reclassification of other comprehensive income (loss) - equity method investment	-	-	-	2,132	-	2,132
Net loss	-	-	-	-	(107,436)	(107,436)
Balance at March 31, 2024	96,333,373	10	2,802,889	(947)	(1,765,815)	1,036,137
Issuance of common stock through at-the-market offerings, net of issuance costs of $14	1,592,823	-	38,399	-	-	38,399
Exercise of stock options	79,512	-	1,179	-	-	1,179
Vesting of restricted stock units	195,691	-	-	-	-	-
Issuance of shares under employee stock purchase plan	87,751	-	1,669	-	-	1,669
Stock-based compensation	-	-	40,861	-	-	40,861
Other comprehensive income (loss) - unrealized loss on marketable securities	-	-	-	(208)	-	(208)
Net loss	-	-	-	-	(146,975)	(146,975)
Balance at June 30, 2024	98,289,150	10	2,884,997	(1,155)	(1,912,790)	971,062
Issuance of common stock through at-the-market offerings, net of issuance costs of $14	3,201,609	-	80,497	-	-	80,497
Exercise of stock options	181,490	-	2,697	-	-	2,697
Vesting of restricted stock units	124,116	-	-	-	-	-
Stock-based compensation	-	-	39,619	-	-	39,619
Other comprehensive income (loss) - unrealized gain on marketable securities	-	-	-	4,452	-	4,452
Net loss	-	-	-	-	(135,712)	(135,712)
Balance at September 30, 2024	101,796,365	$ 10	$ 3,007,810	$ 3,297	$ (2,048,502)	$ 962,615

	Common Shares	Common Amount	Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2022	87,103,007	$ 9	$ 2,420,223	$ (7,461)	$ (1,177,187)	$ 1,235,584
Issuance of common stock through at-the-market offerings, net of issuance costs of $62	35,349	-	1,466	-	-	1,466
Contingent consideration paid to Rewrite Holders	567,045	-	24,126	-	-	24,126
Exercise of stock options	48,353	-	755	-	-	755
Vesting of restricted stock units	342,025	-	-	-	-	-
Stock-based compensation	-	-	27,255	-	-	27,255
Other comprehensive income (loss) - unrealized gain on marketable securities	-	-	-	2,989	-	2,989
Other comprehensive income (loss) - unrealized gain on equity method investment	-	-	-	1,794	-	1,794
Net loss	-	-	-	-	(103,126)	(103,126)
Balance at March 31, 2023	88,095,779	9	2,473,825	(2,678)	(1,280,313)	1,190,843
Exercise of stock options	30,371	-	465	-	-	465
Vesting of restricted stock units	151,853	-	-	-	-	-
Issuance of shares under employee stock purchase plan	69,631	-	2,051	-	-	2,051
Stock-based compensation	-	-	36,400	-	-	36,400
Other comprehensive income (loss) - unrealized loss on marketable securities	-	-	-	(1,482)	-	(1,482)
Other comprehensive income (loss) - unrealized gain on equity method investment	-	-	-	292	-	292
Net loss	-	-	-	-	(123,681)	(123,681)
Balance at June 30, 2023	88,347,634	9	2,512,741	(3,868)	(1,403,994)	1,104,888
Issuance of common stock through at-the-market offerings, net of issuance costs of $81	405,332	-	14,718	-	-	14,718
Exercise of stock options	241,123	-	4,384	-	-	4,384
Vesting of restricted stock units	103,732	-	-	-	-	-
Equity-based compensation	-	-	35,352	-	-	35,352
Other comprehensive income (loss) - unrealized gain on marketable securities	-	-	-	142	-	142
Other comprehensive income (loss) - unrealized gain on equity method investment	-	-	-	154	-	154
Net loss	-	-	-	-	(122,224)	(122,224)
Balance at September 30, 2023	89,097,821	$ 9	$ 2,567,195	$ (3,572)	$ (1,526,218)	$ 1,037,414

See notes to condensed consolidated financial statements.

INTELLIA THERAPEUTICS, INC.
Condensed Consolidated Statements of Cash Flows (unaudited)
(Amounts in thousands)

	Nine Months Ended September 30,	
	2024	**2023**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (390,123)	$ (349,031)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	7,719	6,510
(Gain) loss on disposal of property and equipment	(76)	5
Stock-based compensation	114,656	99,007
Accretion of investment discounts and premiums	(14,215)	(19,590)
(Recognition) deferral of equity method investment intra-entity profit on sales	(20,967)	6,624
Change in fair value of investments, net	29,483	-
Loss from equity method investment	-	10,905
Change in fair value of contingent consideration	-	100
Changes in operating assets and liabilities:		
Accounts receivable	27,602	(2,723)
Prepaid expenses and other current assets	4,643	(11,806)
Operating lease right-of-use assets	15,044	14,148
Other assets	1,476	(836)
Accounts payable	5,364	(1,419)
Accrued expenses	(14,336)	(3,008)
Deferred revenue	(16,231)	(37,705)
Operating lease liabilities	(13,724)	(12,213)
Net cash used in operating activities	(263,685)	(301,032)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	(4,797)	(12,465)
Purchases of marketable securities	(766,471)	(754,689)
Sales and maturities of marketable securities	745,270	689,868
Net cash used in investing activities	(25,998)	(77,286)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Net proceeds from issuance of common stock through at-the-market offerings	176,929	16,184
Proceeds from options exercised	4,832	5,604
Issuance of shares through employee stock purchase plan	1,669	2,051
Net cash provided by financing activities	183,430	23,839
Net decrease in cash, cash equivalents and restricted cash equivalents	(106,253)	(354,479)
Cash, cash equivalents and restricted cash equivalents, beginning of period	240,353	535,463
Cash, cash equivalents and restricted cash equivalents, end of period	$ 134,100	$ 180,984
Reconciliation of cash, cash equivalents and restricted cash equivalents to condensed consolidated balance sheet:		
Cash and cash equivalents	$ 120,495	$ 168,027
Restricted cash equivalents, included in investments and other assets	13,605	12,957
Total cash, cash equivalents and restricted cash equivalents	$ 134,100	$ 180,984
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Purchases of property and equipment unpaid at period end	$ 374	$ 1,552
Proceeds from option exercises unpaid at period end	1,002	-
Non-cash trade-in of property and equipment	99	-
Shares issued for Rewrite contingent consideration	-	24,126

See notes to condensed consolidated financial statements.

INTELLIA THERAPEUTICS, INC.
Notes to Condensed Consolidated Financial Statements (unaudited)

1. Overview and Basis of Presentation

Intellia Therapeutics, Inc. ("Intellia" or the "Company") is a leading clinical-stage gene editing company, focused on developing potentially curative therapeutics using CRISPR/Cas9-based technologies. CRISPR/Cas9, an acronym for Clustered, Regularly Interspaced Short Palindromic Repeats ("CRISPR")/CRISPR associated 9 ("Cas9"), is a technology for genome editing, the process of altering selected sequences of genomic deoxyribonucleic acid ("DNA"). To fully realize the transformative potential of CRISPR/Cas9-based technologies, Intellia is building a full-spectrum gene editing company, by leveraging its modular platform, to advance *in vivo* and *ex vivo* therapies for diseases with high unmet need by pursuing two primary approaches. For *in vivo* applications to address genetic diseases, the Company deploys CRISPR/Cas9 as the therapy. The Company's *in vivo* programs use CRISPR to enable precise editing of disease-causing genes directly inside the human body. In addition, the Company is advancing *ex vivo* applications to address immuno-oncology and autoimmune diseases, where it uses CRISPR/Cas9 as the tool to create the engineered cell therapy. For its *ex vivo* programs, CRISPR/Cas9 is used to engineer human cells outside the body. The Company's deep scientific, technical and clinical development experience, along with its robust intellectual property ("IP") portfolio, have enabled it to unlock broad therapeutic applications of CRISPR/Cas9 and related technologies to create new classes of genetic medicine.

The condensed consolidated financial statements of the Company included herein have been prepared, without audit, pursuant to the rules and regulations of the Securities and Exchange Commission ("SEC"). Certain information and footnote disclosures normally included in annual financial statements prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP") have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these condensed consolidated financial statements should be read in conjunction with the financial statements and notes thereto included in the Company's Annual Report on Form 10-K ("Annual Report") for the year ended December 31, 2023.

The unaudited condensed consolidated financial statements include the accounts of Intellia Therapeutics, Inc. and its wholly- owned subsidiary, Intellia Securities Corp. All intercompany balances and transactions have been eliminated in consolidation. Comprehensive loss is comprised of net loss, unrealized gain/loss on marketable securities and other comprehensive gain/loss from equity method investment.

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates, judgments and assumptions that affect the amounts reported in the financial statements and accompanying notes. Significant estimates in these condensed consolidated financial statements have been made in connection with the calculation of revenues, research and development expenses, valuation of equity and fair value method investments, contingent consideration and stock-based compensation expense. The Company bases its estimates on historical experience and various other assumptions that management believes to be reasonable under the circumstances at the time such estimates are made. Actual results could differ from those estimates. The Company periodically reviews its estimates in light of changes in circumstances, facts and experience.

The effects of material revisions in estimates, if any, would be reflected in the condensed consolidated financial statements prospectively from the date of the change in estimate.

In the opinion of management, the information furnished reflects all adjustments, all of which are of a normal and recurring nature, necessary for a fair presentation of the results for the reported interim periods. The Company considers events or transactions that occur after the balance sheet date but before the financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The results of operations for interim periods are not necessarily indicative of results to be expected for the full year or any other interim period.

Liquidity

Since its inception through September 30, 2024, the Company has raised an aggregate of $2,758.3 million to fund its operations through its initial public offering ("IPO") and concurrent private placements, follow-on public offerings, at-the-market offerings and the sale of convertible preferred stock, as well as through its collaboration agreements. The Company expects that its cash, cash equivalents and marketable securities as of September 30, 2024 will enable the Company to fund its ongoing operating expenses and capital expenditure requirements for at least the twelve-month period following the issuance of these condensed consolidated financial statements.

2. Summary of Significant Accounting Policies

The Company's significant accounting policies are described in Note 2, "Summary of Significant Accounting Policies" to the consolidated financial statements included in the Annual Report for the year ended December 31, 2023. There have been no material changes to these policies during the nine months ended September 30, 2024.

Recent Issued Accounting Pronouncements Not Yet Effective

In November 2023, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2023-07, *Segment Reporting - Improvements to Reportable Segment Disclosures.* The ASU requires disclosure of incremental segment information on an annual and interim basis and also requires companies with a single reportable segment to provide all disclosures required by this ASU and all existing segment disclosures in Accounting Standard Codification ("ASC") 280, *Segment Reporting*. The ASU is effective for fiscal years beginning after December 15, 2023, and interim periods beginning after December 15, 2024. The Company is currently evaluating the impact of adopting this ASU on its consolidated financial statements and disclosures.

In December 2023, the FASB issued ASU No. 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures*. This ASU updates income tax disclosure requirements primarily by requiring specific categories and greater disaggregation within the rate reconciliation and disaggregation of income taxes paid by jurisdiction. This ASU is effective for annual periods beginning after December 15, 2024 and is applicable to the Company's fiscal year beginning January 1, 2025, with early application permitted. The Company is currently evaluating the impact of adopting this ASU on its consolidated financial statements and disclosures.

3. Marketable Securities

The following table summarizes the Company's available-for-sale marketable securities:

	September 30, 2024			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(In thousands)			
Marketable securities:				
U.S. Treasury and other government-backed securities	$ 432,997	$ 1,345	$ (53)	$ 434,289
Financial institution debt securities	248,197	1,437	(27)	249,607
Corporate debt securities	104,174	584	(19)	104,739
Other asset-backed securities	35,521	30	-	35,551
Total	$ 820,889	$ 3,396	$ (99)	$ 824,186

	December 31, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(In thousands)			
Marketable securities:				
U.S. Treasury and other government-backed securities	$ 382,260	$ 302	$ (254)	$ 382,308
Financial institution debt securities	246,270	92	(243)	246,119
Corporate debt securities	97,490	53	(135)	97,408
Other asset-backed securities	59,453	75	(24)	59,504
Total	$ 785,473	$ 522	$ (656)	$ 785,339

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. There were no material realized gains or losses in the nine months ended September 30, 2024 or for the year ended December 31, 2023. The Company generally does not intend to sell any investments prior to recovery of their amortized cost basis for any investment in an unrealized loss position. As such, the Company has classified these losses as temporary in nature.

The Company's available-for-sale securities that are classified as short-term marketable securities in the condensed consolidated balance sheet mature within one year or less as of the balance sheet date. Available-for-sale securities that are classified as noncurrent in the condensed consolidated balance sheet are those that mature after one year but within five years from the balance sheet date and that the Company does not intend to dispose of within the next twelve months. At September 30, 2024 and

December 31, 2023, the Company did not hold any marketable securities that matured beyond five years of the balance sheet date.

4. Fair Value Measurements

The Company classifies fair value-based measurements using a three-level hierarchy that prioritizes the inputs used to measure fair value. This hierarchy requires entities to maximize the use of observable inputs and minimize the use of unobservable inputs. The three levels of inputs used to measure fair value are as follows: Level 1, quoted market prices (unadjusted) in active markets for identical assets or liabilities; Level 2, observable inputs other than quoted market prices included in Level 1, such as quoted market prices for markets that are not active or other inputs that are observable or can be corroborated by observable market data; and Level 3, unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities, including certain pricing models, discounted cash flow methodologies and similar techniques that use significant unobservable inputs.

The Company's financial assets recognized at fair value on a recurring basis consisted of the following:

	September 30, 2024			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Assets				
Cash equivalents and restricted cash equivalents	$ 93,355	$ 93,355	$ -	$ -
Marketable securities:				
U.S. Treasury and other government-backed securities	434,289	199,705	234,584	-
Financial institution debt securities	249,607	-	249,607	-
Corporate debt securities	104,739	-	104,739	-
Other asset-backed securities	35,551	-	35,551	-
Total marketable securities	824,186	199,705	624,481	-
Investment in Kyverna Therapeutics, Inc.	5,740	5,740	-	-
Total assets	$ 923,281	$ 298,800	$ 624,481	$ -

	December 31, 2023			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Assets				
Cash equivalents and restricted cash equivalents	$ 136,254	$ 136,254	$ -	$ -
Marketable securities:				
U.S. Treasury and other government-backed securities	382,308	120,556	261,752	-
Financial institution debt securities	246,119	-	246,119	-
Corporate debt securities	97,408	-	97,408	-
Other asset-backed securities	59,504	-	59,504	-
Total marketable securities	785,339	120,556	664,783	-
Total assets	$ 921,593	$ 256,810	$ 664,783	$ -

Certain of the Company's financial assets, including cash equivalents, restricted cash equivalents and marketable securities, have been initially valued at the transaction price, and subsequently revalued at the end of each reporting period, utilizing third party pricing services or other observable market data. The pricing services utilize industry standard valuation models and observable market inputs to determine value.

Other financial instruments, including accounts receivable, accounts payable and accrued expense, are carried at cost, which approximates fair value due to the short duration and term to maturity.

The Company has determined that the estimated fair value of its investment in Kyverna Therapeutics, Inc. ("Kyverna"), a publicly traded company, is reported as Level 1 as it is valued at a quoted market price in an active market. The investment in Kyverna is classified within "investments and other assets" in the condensed consolidated balance sheets. Refer to Note 8 for further details.

Other Investments

The Company's other investments include investments in AvenCell Therapeutics, Inc. ("AvenCell") and SparingVision SAS ("SparingVision"). These investments are accounted for under ASC 321, *Investments in Equity Securities* ("ASC 321") using the measurement alternative at cost minus impairment with adjustments for changes in observable prices. The Company previously accounted for the AvenCell investment under the equity method; refer to Note 8 for further details. The Company monitors any events or changes in circumstances that may have a significant effect on the fair value of investments, either due to impairment or based on observable price changes, and records adjustments as needed. These investments are classified as Level 3 assets and are not included in the fair value table above as they are not valued at fair value on a recurring basis.

5. Accrued Expenses

Accrued expenses consisted of the following:

	September 30, 2024	December 31, 2023
	(In thousands)	
Accrued research and development	$ 24,325	$ 27,411
Employee compensation and benefits	20,551	26,615
Accrued legal and professional expenses	2,677	2,063
Accrued construction costs	1,349	6,891
Accrued other	2,304	4,037
Total accrued expenses	$ 51,206	$ 67,017

6. Commitments and Contingencies

Litigation

From time to time, the Company may be involved in legal and administrative proceedings and claims of various types. In some actions, the claimants seek damages, as well as other relief, which, if granted, would require significant expenditures. The Company records a liability in its consolidated financial statements for these matters when a loss is known or considered probable and the amount can be reasonably estimated. The Company reviews these estimates each accounting period as additional information is known and adjusts the loss provision when appropriate. If a matter is both probable to result in a liability to the Company and the amount of the loss can be reasonably estimated, the Company estimates and discloses the possible loss or range of loss. If the loss is not probable or cannot be reasonably estimated, a liability is not recorded in its consolidated financial statements.

BlueAllele Corp. v. Intellia Therapeutics, Inc.

On July 8, 2024, BlueAllele Corp. ("BlueAllele") filed a complaint alleging infringement by the Company of various patents in the U.S. District Court for the District of Delaware. Specifically, BlueAllele alleges that the Company's experimentation, basic research, identification, optimization, manufacturing and/or use of bi-directional insertion template technology infringes the asserted patents and seeks unspecified compensatory damages and an injunction against the alleged infringing activities. On September 12, 2024, the Company filed a motion to dismiss the complaint. BlueAllele responded to the motion to dismiss on October 23, 2024. At this stage, the Company is unable to determine the likelihood of an unfavorable outcome or estimate the amount or range of potential loss, if any.

Except as noted above, there have been no material changes to any outstanding litigation, nor is the Company a party to any material new litigation, since December 31, 2023.

License Agreements

The Company is party to license agreements, which may include contingent payments. These payments will become payable if and when certain development, regulatory and commercial milestones are achieved. As of September 30, 2024, the satisfaction and timing of the contingent payments is uncertain and not reasonably estimable.

7. Collaborations and Other Arrangements

To accelerate the development and commercialization of CRISPR/Cas9-based products in multiple therapeutic areas, the Company has formed, and intends to seek other opportunities to form, strategic alliances with collaborators who can augment its

leadership in CRISPR/Cas9 therapeutic development. As of September 30, 2024, the Company's accounts receivable were related to its collaborations with Regeneron Pharmaceuticals, Inc. ("Regeneron"), SparingVision and AvenCell, and the Company's contract liabilities were related to its collaborations with Regeneron and SparingVision. As of December 31, 2023, the Company's accounts receivable were related to its collaborations with Regeneron, SparingVision, AvenCell and Kyverna and the Company's contract liabilities were related to its collaborations with Regeneron and SparingVision.

The following table presents changes in the Company's accounts receivable and contract liabilities (in thousands):

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Nine months ended September 30, 2024				
Accounts receivable	$ 36,456	$ 19,422	$ (47,024)	$ 8,854
Contract liabilities - deferred revenue	$ 60,993	$ -	$ (16,231)	$ 44,762

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Nine months ended September 30, 2023				
Accounts receivable	$ 3,768	$ 15,287	$ (12,564)	$ 6,491
Contract liabilities - deferred revenue	$ 63,771	$ -	$ (37,705)	$ 26,066

During the nine months ended September 30, 2024 and 2023, the Company recognized the following revenues as a result of changes in the contract liability balance (in thousands):

	Nine Months Ended September 30,	
Revenue recognized in the period from:	**2024**	**2023**
Amounts included in the contract liability at the beginning of the period	$ 16,231	$ 31,081

The Company has not incurred significant expenses to obtain collaboration agreements and costs to fulfill those contracts do not generate or enhance resources of the Company. As such, no costs to obtain or fulfill a contract have been capitalized in any period.

Regeneron Pharmaceuticals, Inc.

In April 2016, the Company entered into a license and collaboration agreement with Regeneron (as amended from time to time, the "2016 Regeneron Agreement"). In October 2023, Regeneron exercised its one-time option to extend the technology collaboration term for an additional two years, until April 2026, in exchange for a nonrefundable payment of $30.0 million, which was received by the Company in April 2024. In September 2023, Regeneron and Intellia further expanded the research collaboration (the "2023 Regeneron Amendment") to develop additional *in vivo* CRISPR-based gene editing therapies focused on neurological and muscular diseases.

In 2018, the Company entered into a co-development and co-promotion ("Co/Co") agreement with Regeneron for transthyretin ("ATTR") amyloidosis (the "ATTR Co/Co"). In May 2020, the Company entered into co-development and co-funding agreements for the treatment of hemophilia A and hemophilia B (the "Hemophilia Co/Co") agreements. In March 2024, the Company notified Regeneron that it was opting out of its hemophilia B Co/Co agreement. The Company continued to have obligations under the hemophilia B Co/Co agreement until the agreement ended in September 2024. The Company will continue to support Regeneron with the development of gene editing products directed to hemophilia B, as applicable, under the 2016 Regeneron Agreement. That agreement will control the parties' obligations to develop and commercialize gene editing products directed to hemophilia B. Under the 2016 Regeneron Agreement, the Company may be eligible to receive up to $320.0 million in milestone payments and royalties in the high-single digits to low teens, which royalties are potentially subject to various reductions, offsets and upstream payment obligations.

Since December 31, 2023, there have been no material changes to the key terms of the 2016 Regeneron Agreement, ATTR Co/Co, Hemophilia Co/Co, or 2023 Regeneron Amendment (the "Regeneron Agreements"), other than as described above.

The Company recognized collaboration revenue related to the Regeneron Agreements of $8.3 million and $22.1 million during the three and nine months ended September 30, 2024, respectively, and $9.3 million and $23.5 million during the three and nine months ended September 30, 2023, respectively, in the condensed consolidated statements of operations and comprehensive loss. This includes approximately $6.4 million and $16.1 million during the three and nine months ended September 30, 2024, respectively, and $5.5 million and $14.2 million during the three and nine months ended September 30, 2023, respectively, primarily representing payments due from Regeneron pursuant to the ATTR Co/Co. These revenues are offset in part by contra-revenue related to the Hemophilia Co/Co agreements amounting to approximately $4.0 million and $11.6 million during the three and nine months ended September 30, 2024, respectively, and $1.8 million and $7.6 million during the three and nine months ended September 30, 2023, respectively.

As of September 30, 2024, there was $31.6 million of the aggregate transaction price remaining to be recognized through April 2026, the remaining period of the 2016 Regeneron Agreement. As of September 30, 2024 and December 31, 2023, the Company had accounts receivable of $8.1 million and $35.7 million, respectively, and deferred revenue of $31.6 million and $47.1 million, respectively, related to the Regeneron Agreements.

SparingVision SAS

In October 2021, the Company and SparingVision, a genomic medicine company developing vision saving treatments for ocular diseases, entered into a license and collaboration agreement (the “SparingVision LCA”) to develop novel genomic medicines utilizing CRISPR/Cas9 technology for the treatment of ocular diseases.

Since December 31, 2023, there have been no material changes to the key terms of the SparingVision LCA agreement.

The Company recognized collaboration revenue related to the SparingVision LCA of approximately $0.6 million and $1.7 million, respectively, for the three and nine months ended September 30, 2024 and $0.4 million and $1.3 million, respectively, for the three and nine months ended September 30, 2023, in the condensed consolidated statements of operations and comprehensive loss. As of September 30, 2024 and December 31, 2023, the Company had $0.3 million and $0.5 million in accounts receivable, respectively, related to the SparingVision LCA. As of September 30, 2024 and December 31, 2023, the Company had deferred revenue of $13.2 million and $13.9 million, respectively, related to the SparingVision LCA, which is expected to be recognized over a six to nine year period from the signing of the agreement.

ReCode Therapeutics, Inc. (“ReCode”)

On February 14, 2024, the Company entered into a license, collaboration and option agreement with ReCode (the “ReCode LCA”), a clinical-stage genetic medicines company, to develop novel genomic medicines for the treatment of cystic fibrosis (“CF”). The ReCode LCA leverages the Company’s proprietary CRISPR-based gene editing platform, including its DNA writing technology, and ReCode’s proprietary Selective Organ Targeting (“SORT”) lipid nanoparticle delivery platform to precisely correct one or more CF disease-causing gene mutations. As part of the agreement, the companies will focus initial research efforts on therapeutic approaches that address CF for patients who have limited or no treatment options available, with the opportunity to expand the scope of the collaboration in later phases. The Company will be responsible for the design of the editing strategy and research-grade components for the investigational therapies. ReCode will lead the subsequent preclinical and clinical development and worldwide commercialization for certain programs arising from the collaboration. The Company also has an option to lead commercialization in the U.S. for certain programs (the “Co/Co option”).

The ReCode LCA did not include an exchange of upfront consideration between the parties. The Company will be eligible to receive pre-specified development and commercial milestone payments, up to $262.0 million per product, as well as single digit royalties on potential sales. Certain milestone and royalty payments may be removed or reduced for a product if the Company exercises the Co/Co option. The Company did not recognize any revenue from the ReCode LCA during the three or nine months ended September 30, 2024.

Other Agreements

The Company has existing license and collaboration agreements with AvenCell, Kyverna, and ONK Therapeutics, Ltd. (“ONK”). Since December 31, 2023, there have been no material changes to the key terms of the AvenCell, Kyverna and ONK license and collaboration agreements. During the three and nine months ended September 30, 2024, the Company recognized $0.2 million related to materials shipped in accordance with the AvenCell license and collaboration agreement (the “AvenCell LCA”) as well as $21.0 million of previously eliminated intra-entity profit related to the AvenCell LCA in the condensed consolidated

statements of operations and comprehensive loss. See Note 8 for further details. The Company did not recognize material revenue from the Kyverna and ONK agreements during the three and nine months ended September 30, 2024. During the three months ended September 30, 2023, the Company recognized $1.9 million, $0.1 million and $0.2 million in revenue related to AvenCell, Kyverna and ONK, respectively. During the nine months ended September 30, 2023, the Company recognized $12.7 million, $0.5 million and $0.2 million in revenue related to AvenCell, Kyverna and ONK, respectively.

8. Investments and Other Assets

Investments and other assets consisted of the following:

	September 30, 2024	December 31, 2023
	(In thousands)	
Investment in Kyverna	$ 5,740	$ 10,000
Other investments	24,213	14,760
Restricted cash equivalents, long-term	13,605	13,605
Prepaid expenses and other assets, long-term	3,230	4,518
Total investments and other assets	$ 46,788	$ 42,883

Kyverna Therapeutics, Inc.

In February 2024, Kyverna completed an initial public offering of its common stock (the "Kyverna IPO"). Prior to the Kyverna IPO, the Company accounted for its investment in Kyverna using the measurement alternative as Kyverna was a private company with no readily observable transaction price, and the investment was valued at $10.0 million as of December 31, 2023. As of September 30, 2024, the Company's investment in Kyverna is valued at $5.7 million. The Company recognized an unrealized loss of $3.1 million and $4.3 million, recorded within "change in fair value of investments, net" in the condensed consolidated statement of operations and comprehensive loss during the three and nine months ended September 30, 2024, respectively, associated with changes in the fair value of Kyverna's common stock.

AvenCell Therapeutics, Inc.

As of September 30, 2024 and December 31, 2023, the Company held a 33.33% equity interest in AvenCell. As of December 31, 2023, the Company accounted for its investment using the equity method of accounting, as the Company had significant influence, but not control, over AvenCell, and the investment was valued at $11.8 million. During the first quarter of 2024, in conjunction with the completion of a debt financing, AvenCell increased the size of their board, with a single investor having control over AvenCell's operational and financial decisions. From that point forward, the Company no longer had the ability to exercise significant influence over AvenCell, and therefore the Company's investment in AvenCell is accounted for in accordance with ASC 321 and AvenCell is no longer considered to be a related party.

The transition from equity method accounting to ASC 321 required the Company to reclassify $2.1 million from accumulated other comprehensive loss amounts previously recognized as a result of the investment in AvenCell to the carrying value of the investment in AvenCell and recognize $21.0 million of previously eliminated intra-entity profit as "collaboration revenue" in the condensed consolidated statement of operations and comprehensive loss during the first quarter of 2024. The Company also considered whether there was an indication that the investment was impaired, and recorded an impairment of $25.3 million within "change in fair value of investments, net" in the condensed consolidated statement of operations and comprehensive loss during that period. This impairment was caused by AvenCell's financial condition, indicators of fair value based on the completion of the debt financing, and an executed term sheet for further financing, which indicated that the fair value of the investment was less than its carrying value. The Company used a market approach to value the investment, which is a Level 3 measurement in the fair value hierarchy.

In addition to the $21.0 million of previously eliminated intra-entity profit noted above that was recognized during the nine months ended September 30, 2024, the Company recognized $0.2 million related to materials shipped in accordance with the AvenCell LCA during that period. During the three and nine months ended September 30, 2023, the Company recognized $1.9 million and $12.7 million in revenue, respectively, related to the AvenCell LCA. The Company had $0.4 million and $0.2 million, respectively, in accounts receivable as of September 30, 2024 and December 31, 2023. The Company also had $1.0 million in accrued expenses related to the AvenCell agreements as of both September 30, 2024 and December 31, 2023.

As of September 30, 2024, the carrying value of the Company's investment in AvenCell, included within "Other investments" in the table above, was $9.6 million.

SparingVision SAS

As of September 30, 2024, the fair value of the Company's investment in SparingVision, included within "Other investments" in the table above, was $14.6 million. There have been no material changes in the valuation of the SparingVision investment as of September 30, 2024.

9. Leases

The Company leases approximately 230,000 square feet of real estate, including laboratory and office space in Cambridge, Massachusetts and the surrounding areas. The Company's leases have remaining terms ranging from one to approximately nine years. Certain leases include options to renew, exercised at the Company's sole discretion, with varying renewal terms that can extend the lease term for an additional three to five years. All of the Company's leases qualify as operating leases.

Separately, the Company entered into an agreement in February 2022, later amended in June 2023, to lease approximately 140,000 square feet of office, general laboratory and planned good manufacturing practice ("GMP") manufacturing space at 840 Winter Street in Waltham, Massachusetts (the "840 Winter Lease"). As of September 30, 2024, the Company had not taken control of the premises and therefore there are no right of use assets or liabilities recorded related to the 840 Winter Lease under ASC 842, *Leases (Topic 842)* ("ASC 842"). The 840 Winter Lease is expected to commence in the fourth quarter of 2024.

10. Stock-Based Compensation

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
	(In thousands)			
Research and development	$ 24,224	$ 21,235	$ 69,824	$ 60,517
General and administrative	15,395	14,117	44,832	38,490
Total	$ 39,619	$ 35,352	$ 114,656	$ 99,007

Stock Option and Incentive Plans

In April 2016, the Company adopted the Amended and Restated 2015 Stock Option and Incentive Plan (the "2015 Plan"). The 2015 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock awards ("RSAs"), restricted stock units ("RSUs") and other stock-based awards. Recipients of incentive stock options and non-qualified stock options are eligible to purchase shares of the Company's common stock at an exercise price equal to the fair value of such stock on the grant date. As of September 30, 2024, there were 4,808,720 shares available for future issuance under the 2015 Plan. The number of shares reserved for issuance under the 2015 Plan will be cumulatively increased on each January 1st by four percent of the number of shares of stock issued and outstanding on the immediately preceding December 31st or such lesser number of shares of stock as determined by the board of directors.

In June 2024, the Company adopted the 2024 Inducement Plan (the "Inducement Plan"). The Inducement Plan provides for the grant of non-qualified stock options, stock appreciation rights, RSAs, RSUs, unrestricted stock awards and dividend equivalent rights to individuals who are not employed by the Company. Recipients of non-qualified stock options are eligible to purchase shares of the Company's common stock at an exercise price equal to the fair value of such stock on the grant date. In accordance with the Inducement Plan, 850,000 shares of common stock were reserved for future issuance; there were 500,826 shares available for future issuance under the Inducement Plan as of September 30, 2024.

Restricted Stock Units

The following table summarizes the Company's RSU activity for the nine months ended September 30, 2024:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Unvested restricted stock units as of December 31, 2023	4,041,753	$ 50.40
Granted	3,326,772	33.89
Vested	(1,335,350)	51.56
Cancelled	(582,581)	43.50
Unvested restricted stock units as of September 30, 2024	5,450,594	$ 40.77

Restricted Stock Units - Service Awards

The Company awards RSUs with a service condition to all employees upon hire and as part of their annual grant. RSUs with a service condition granted under the 2015 Plan in 2024 and 2023 and the Inducement Plan in 2024 generally vest as to one-third on the first anniversary of the original vesting date, with the balance vesting annually over the remaining two years.

In March 2024, the Company granted 2,157,921 RSUs with a service condition to employees as part of their annual grant, which have the potential to vest over a period of three years. The weighted average grant date fair value of these RSUs was $32.66 and the vesting start date for these RSUs was January 1, 2024.

In March 2023, the Company granted 2,195,135 RSUs with a service condition to employees as part of their annual grant, which have the potential to vest over a period of three years. The weighted average grant date fair value of these RSUs was $40.75 and the vesting start date for these RSUs was January 1, 2023.

Unvested restricted stock units as of September 30, 2024 in the table above includes 4,464,378 RSUs that are service-based.

Restricted Stock Units - Market Awards

In 2024, 2023 and 2022, market-based RSUs were granted to senior executives. These RSUs have the potential to vest after a period of three years, with a vesting start date of January 1, 2024, 2023 and 2022, respectively, and the number of shares to be delivered will depend on the Company's Total Shareholder Return ("TSR"), a market condition, over that period relative to a defined group of biotechnology companies. The number of market-based RSUs granted in the nine months ended September 30, 2024, 2023 and 2022 was 286,084, 181,743 and 55,144, respectively. The grant date fair value for the market-based RSUs, calculated using a Monte Carlo valuation model, was $51.12, $68.55 and $126.49, respectively. The following assumptions were used to determine the grant date fair value for the three years, respectively: risk free interest rate: 4.28%, 4.60% and 1.44%; expected volatility: 77.2%, 84.34% and 82.53%. The expected term for all grants was approximately 3.0 years; the expected dividend yield was 0.0%.

Unvested restricted stock units as of September 30, 2024 in the table above includes 488,555 RSUs that are market-based.

Restricted Stock Units - Performance-Based Awards with TSR Multiplier

Also in 2024, performance-based RSUs ("PSUs") with a relative TSR modifier were granted to senior executives. The number of PSUs with a relative TSR modifier granted in the nine months ended September 30, 2024 was 486,617. These PSUs, to the extent earned, shall vest on January 1, 2027, and the number of shares to be delivered will be determined based upon the achievement of certain performance goals, which can range from 0% to 200%. Following the determination of the achievement of performance criteria, the amount of shares awarded will be subject to adjustment based on the application of a TSR modifier, which can range from 75% to 125%. The grant date fair value for these PSUs, calculated using a Monte Carlo valuation model, was $36.16. The following assumptions were used to determine the grant date fair value: risk free interest rate: 4.28%; expected volatility: 77.2%; expected term approximately 3.0 years; expected dividend yield: 0.0%. The Company recognizes compensation expense ratably over the required service period based on its estimate of the number of shares that will vest based upon the probability of achieving the performance goals.

Unvested restricted stock units as of September 30, 2024 in the table above includes 453,243 PSUs with a TSR multiplier.

Restricted Stock Units - Performance-Based Awards

In March 2022, the Company granted 66,296 performance-based RSUs to certain non-executive employees that would vest upon obtaining certain scientific milestones. There were two separate tranches, each attached to a different set of milestones. The milestone related to the first tranche, made up of 21,878 RSUs, was achieved in the first quarter of 2023 and these RSUs vested. The remaining performance milestones were considered not probable of achievement as of September 30, 2024 and, therefore, no related stock-based compensation expense was recorded during the period then ending.

Unvested restricted stock units as of September 30, 2024 in the table above includes 44,418 performance-based RSUs.

The weighted-average grant date fair value of all RSUs granted during the three and nine months ended September 30, 2024 was $30.63 and $33.89, respectively. The total fair value of RSUs vested (measured on the date of vesting) for the three and nine months ended September 30, 2024 was $2.8 million and $38.3 million, respectively. The weighted-average grant date fair value of RSUs granted during the three and nine months ended September 30, 2023 was $39.14 and $42.36, respectively. The total fair value of RSUs vested (measured on the date of vesting) for the three and nine months ended September 30, 2023 was $4.2 million and $22.5 million, respectively.

As of September 30, 2024, there was $133.3 million of unrecognized stock-based compensation expense related to all RSUs that are expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 1.7 years.

Stock Options

The weighted average grant date fair value of options, estimated as of the grant date using the Black-Scholes option pricing model, was $16.98 and $21.21 per option for those options granted during the three and nine months ended September 30, 2024, respectively, and $28.92 per option for those options granted during the nine months ended September 30, 2023. There were no options granted during the three months ended September 30, 2023. Weighted average assumptions used to apply this pricing model were as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Risk-free interest rate	4.0%	n/a	4.2%	4.4%
Expected term	6.0 years	n/a	6.0 years	6.0 years
Expected volatility of underlying stock	75.8%	n/a	76.3%	78.7%
Expected dividend yield	0.0%	n/a	0.0%	0.0%

Risk-free Interest Rate. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant with maturities approximately equal to the option's expected term.

Expected Term. The expected term represents the period that stock option awards are expected to be outstanding. For option grants that are considered to be "plain vanilla," the Company determines the expected term using the simplified method. The simplified method deems the term to be the average of the time-to-vesting and the contractual life of the options. The Company uses the simplified method because it does not have sufficient historical option exercise data to provide a reasonable basis upon which to estimate the expected term.

Expected Volatility. Expected volatility is estimated based on actual movements in the Company's stock price over the most recent historical periods, over the expected term of their stock option grants.

Expected Dividend Yield. The Company has not paid cash dividends and has no intention to pay cash dividends in the future.

Stock options generally vest as to one-third on the first anniversary of the original vesting date, with the balance vesting monthly over the remaining two years, unless they contain specific vesting provisions. The maximum term of stock options granted under the 2015 Plan and the Inducement Plan is ten years.

The following is a summary of stock option activity for the nine months ended September 30, 2024:

	Number of Options	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Outstanding at December 31, 2023	5,458,999	$ 50.38	6.65	$ 35,922
Granted	918,161	30.72		
Exercised	(371,736)	15.69		
Forfeited	(526,473)	71.23		
Outstanding at September 30, 2024	5,478,951	$ 47.43	6.52	$ 11,250
Exercisable at September 30, 2024	4,096,828	$ 47.42	5.76	$ 11,250

The total intrinsic value (the amount by which the fair market value exceeded the exercise price) of stock options exercised during the three and nine months ended September 30, 2024 was $1.1 million and $3.1 million, respectively. The total intrinsic value of stock options exercised during the three and nine months ended September 30, 2023 was $4.8 million and $6.6 million, respectively.

As of September 30, 2024, there was $34.5 million of unrecognized compensation cost related to stock options that have not yet vested which are expected to be recognized over a weighted average remaining vesting period of 1.16 years.

Employee Stock Purchase Plan

In May 2016, the Company adopted the 2016 Employee Stock Purchase Plan (the “2016 Plan”). The 2016 Plan allows eligible employees to purchase shares of the Company’s common stock on the last day of each predetermined six-month offering period at 85% of the lower of the fair market value per share at the beginning or end of the applicable offering period. The 2016 Plan provides for six-month offering periods beginning in January and July of each year.

As of September 30, 2024, there were 989,736 shares available for future issuance under the 2016 Plan. The number of shares reserved for issuance under the 2016 Plan will be cumulatively increased on each January 1st by the lesser of a) one percent of the number of shares of common stock issued and outstanding on the immediately preceding December 31st, b) 500,000 shares of common stock, or c) such lesser number of shares of common stock as determined by the board of directors.

During the nine months ended September 30, 2024 and 2023 the Company issued 87,751 and 69,631 shares of common stock under the 2016 Plan, respectively. The weighted-average purchase prices of shares issued under the 2016 Plan were $19.02 and $29.45 per share for the nine months ended September 30, 2024 and 2023, respectively.

The fair value of shares under the 2016 Plan was estimated at the beginning of the offering period using a Black-Scholes option-pricing model with the following assumptions:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Risk-free interest rate	5.37%	5.53%	5.24%-5.37%	4.7%-5.53%
Expected term	0.5 years	0.5 years	0.5 years	0.5 years
Expected volatility of underlying stock	59.0%	60.4%	56.7%-59.0%	60.4%-69.2%
Expected dividend yield	0.0%	0.0%	0.0%	0.0%

11. Loss Per Share

The Company calculates basic loss per share by dividing net loss for each respective period by the weighted average number of common shares outstanding for each respective period. The Company computes diluted loss per share after giving consideration to the dilutive effect of stock options and unvested restricted stock units that are outstanding during the period, except where such securities would be anti-dilutive.

Basic and diluted loss per share was calculated as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
	(In thousands)			
Net loss	$ (135,712)	$ (122,224)	$ (390,123)	$ (349,031)
Weighted average shares outstanding, basic and diluted	101,002	88,645	97,842	88,204
Net loss per share, basic and diluted	$ (1.34)	$ (1.38)	$ (3.99)	$ (3.96)

The following common stock equivalents were excluded from the calculation of diluted loss per share because their inclusion would have been anti-dilutive:

	Three and Nine Months Ended September 30,	
	2024	2023
	(In thousands)	
Unvested restricted stock units	5,451	3,925
Stock options	5,479	5,591
	10,930	9,516

12. Stockholders' Equity

At-the-Market Offering Programs

2022 Sale Agreement

In March 2022, the Company entered into an Open Market Sale Agreement (the "2022 Sale Agreement") with Jefferies LLC ("Jefferies"), under which Jefferies was able to offer and sell, from time to time in "at-the-market" offerings, shares of the Company's common stock having aggregate gross proceeds of up to $400.0 million. In February 2024, the Company entered into an amendment to the 2022 Sale Agreement (the "2022 Sale Agreement, as amended") to increase the size of the at-the-market offering program from $400.0 million to $750.0 million. The Company agreed to pay cash commissions of up to 3.0% of the gross proceeds of sales of common stock under the 2022 Sale Agreement, as amended. Through September 30, 2024, the Company issued 14,522,533 shares of its common stock under the 2022 Sale Agreement, as amended.

During the nine months ended September 30, 2024, the Company issued 7,004,370 shares of its common stock, in a series of sales, at an average price of $25.68 per share, in accordance with the 2022 Sale Agreement, as amended, for aggregate net proceeds of $174.9 million, after payment of cash commissions and approximately $0.2 million related to legal, accounting and other fees in connection with the sales.

As of September 30, 2024, $249.1 million in shares of common stock remain eligible for sale under the 2022 Sale Agreement, as amended.

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

Forward-looking Information

This Quarterly Report on Form 10-Q contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements may be identified by such forward-looking terminology as "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. Our forward-looking statements are based on a series of expectations, assumptions, estimates and projections about our company, are not guarantees of future results or performance and involve substantial risks and uncertainty. We may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements. Our business and our forward-looking statements involve substantial known and unknown risks and uncertainties, including the risks and uncertainties inherent in our statements regarding:

- our ability to execute our clinical study strategy for NTLA-2001, our program for the treatment of transthyretin ("ATTR") amyloidosis, including the ability to successfully complete our global Phase 3 study for ATTR amyloidosis with cardiomyopathy ("ATTR-CM"), to initiate and complete our global Phase 3 study for hereditary ATTR amyloidosis with polyneuropathy ("ATTRv-PN"), or the success of such program;
- our ability to execute our clinical study strategy for NTLA-2002, our program for the treatment of hereditary angioedema ("HAE"), including the ability to successfully complete our global Phase 3 study, generate results supporting the potential of NTLA-2002 to be a functional cure for HAE, file a biologics license application ("BLA") or comparable marketing application within a certain time period, or the success of such program;
- our ability to execute our clinical study strategy for NTLA-3001, our program for the treatment of alpha-1 antitrypsin deficiency ("AATD")-associated lung disease, including the ability to successfully initiate our Phase 1 study and dose the first patient in 2024, or the success of such program;
- our ability to use a modular platform capability or other strategies to efficiently discover and develop product candidates, including by applying learnings from one program to other programs;
- our ability to research, develop or maintain a pipeline of product candidates, including *in vivo* and *ex vivo* product candidates;
- our ability to manufacture or obtain materials for our preclinical and clinical studies, and our product candidates;
- our ability to advance any product candidates into, and successfully complete, clinical studies, including clinical studies necessary for regulatory approval and commercialization, and to demonstrate to the regulators that the product candidates are safe and effective and that their benefits outweigh known and potential risks for the intended patient population;
- our ability to advance our genome editing and therapeutic delivery capabilities, including our therapeutic delivery capabilities for tissues other than the liver;
- the scope of protection we are able to develop, establish and maintain for intellectual property rights, including patents, trade secrets and license rights, covering our product candidates and technology;
- our ability to operate, including commercializing products, without infringing or breaching the proprietary or contractual rights of others;
- the issuance or enforcement of, and compliance with, regulatory requirements and guidance regarding preclinical and clinical studies relevant to genome editing and our product candidates;
- the market acceptance, pricing and reimbursement of our product candidates, if approved;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the potential benefits of strategic agreements, such as collaborations, co-development and co-commercialization, acquisitions, dispositions, mergers, joint ventures, and investment agreements, and our ability to establish and maintain strategic arrangements under favorable terms;

- our ability to acquire and maintain relevant intellectual property licenses and rights, and the scope and terms of such rights;
- developments relating to our licensors, licensees, third parties and ventures from which we derive or license rights, as well as collaborators, competitors and our industry; and
- other risks and uncertainties, including those listed under the caption "Risk Factors."

All of our express or implied forward-looking statements are as of the date of this Quarterly Report on Form 10-Q only. In each case, actual results may differ materially from such forward-looking information. We can give no assurance that such expectations or forward-looking statements will prove to be correct. An occurrence of or any material adverse change in one or more of the risk factors or risks and uncertainties referred to in this Quarterly Report on Form 10-Q or included in our other public disclosures or our other periodic reports or other documents or filings filed with or furnished to the Securities and Exchange Commission (the "SEC") could materially and adversely affect our business, prospects, financial condition and results of operations. Except as required by law, we do not undertake or plan to update or revise any such forward-looking statements to reflect actual results, changes in plans, assumptions, estimates or projections or other circumstances affecting such forward-looking statements occurring after the date of this Quarterly Report on Form 10-Q, even if such results, changes or circumstances make it clear that any forward-looking information will not be realized. Any public statements or disclosures by us following this Quarterly Report on Form 10-Q that modify or impact any of the forward-looking statements contained in this Quarterly Report on Form 10-Q will be deemed to modify or supersede such statements in this Quarterly Report on Form 10-Q.

Management Overview

Intellia Therapeutics, Inc. ("we," "us," "our," "Intellia," or the "Company") is a leading clinical-stage gene editing company, focused on developing potentially curative therapeutics using CRISPR/Cas9-based technologies. CRISPR/Cas9, an acronym for Clustered, Regularly Interspaced Short Palindromic Repeats ("CRISPR")/CRISPR associated 9 ("Cas9"), is a technology for genome editing, the process of altering selected sequences of genomic deoxyribonucleic acid ("DNA"). To fully realize the transformative potential of CRISPR/Cas9-based technologies, we are building a full-spectrum gene editing company, by leveraging our modular platform, to advance *in vivo* and *ex vivo* therapies for diseases with high unmet need by pursuing two primary approaches. For *in vivo* applications to address genetic diseases, we deploy CRISPR/Cas9 as the therapy. Our *in vivo* programs use CRISPR to enable precise editing of disease-causing genes directly inside the human body. In addition, we are advancing *ex vivo* applications to address immuno-oncology and autoimmune diseases, where we use CRISPR/Cas9 as the tool to create the engineered cell therapy. For our *ex vivo* programs, CRISPR/Cas9 is used to engineer human cells outside the body. Our deep scientific, technical and clinical development experience, along with our robust intellectual property ("IP") portfolio, have enabled us to unlock broad therapeutic applications of CRISPR/Cas9 and related technologies to create new classes of genetic medicine.

Our management's discussion and analysis of our financial condition and results of operations are based upon our unaudited condensed consolidated financial statements included in this Quarterly Report on Form 10-Q, which have been prepared by us in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP") for interim periods and with Regulation S-X, promulgated under the Securities Exchange Act of 1934, as amended. This discussion and analysis should be read in conjunction with the unaudited condensed consolidated financial statements and the notes thereto included elsewhere in this Quarterly Report on Form 10-Q as well as in conjunction with the audited financial statements and notes thereto included in our Annual Report on Form 10-K ("Annual Report") for the year ended December 31, 2023.

Treating—and potentially curing—a broad range of severe diseases will require multiple gene editing approaches. With proprietary CRISPR/Cas9-based technology at the core of our platform, we continue to add new capabilities to expand our current solutions for addressing a multitude of life-threatening diseases. These additions include our proprietary base editor and DNA writing technology, as well as novel CRISPR enzymes, which provide us with the capabilities to achieve multiple editing strategies.

We continue to advance our platform's modular solutions and research efforts on genome editing technologies as well as delivery and cell engineering capabilities to generate additional development candidates.

Our mission is to transform the lives of people with severe diseases by developing potentially curative genome editing treatments. We believe we can deliver on our mission and provide long-term benefits for all of our stakeholders by focusing on four key elements:

- Develop curative CRISPR/Cas9-based medicines;
- Advance our science;
- Be the best place to make therapies; and
- Focus on long-term sustainability.

Our strategy is to advance our full-spectrum gene editing company, focused on developing and commercializing curative CRISPR/Cas9-based therapeutics, by leveraging our modular platforms. All of our revenue to date has been collaboration revenue. Since our inception and through September 30, 2024, we have raised an aggregate of approximately $2,758.3 million to fund our operations through our initial public offering ("IPO") and concurrent private placements, follow-on public offerings, at-the-market offerings, and the sale of convertible preferred stock, as well as through our collaboration agreements.

Our lead *in vivo* candidates, NTLA-2001 for the treatment of transthyretin ("ATTR") amyloidosis and NTLA-2002 for the treatment of hereditary angioedema ("HAE"), are the first CRISPR/Cas9-based therapy candidates to be administered systemically, via intravenous infusion, for precision editing of a gene in a target tissue in humans. In addition, we are advancing multiple *ex vivo* programs, wholly owned and in collaboration with partners, for the treatment of immuno-oncology and autoimmune diseases.

Our Pipeline

In Vivo *Programs*

Our selection criteria include identifying diseases that originate in the liver; have well-defined mutations that can be addressed by a knockout or insertion approach; have readily measurable therapeutic endpoints with observable clinical responses; and for which effective treatments are absent, limited or unduly burdensome. Our initial *in vivo* indications target genetic liver diseases, including our ATTR amyloidosis, HAE and alpha-1 antitrypsin deficiency ("AATD") development programs. Our current efforts on *in vivo* delivery focus on the use of lipid nanoparticles ("LNPs") for delivery of the CRISPR/Cas9 complex to the liver.

Transthyretin ("ATTR") Amyloidosis Program

NTLA-2001, now known as nexiguran ziclumeran ("nex-z"), is an investigational *in vivo* CRISPR-based therapy designed to inactivate the transthyretin (*"TTR"*) gene in liver cells, thereby preventing the production of TTR protein for the treatment of ATTR amyloidosis. Nex-z offers the possibility of halting and reversing the disease by driving a deep, consistent and potentially lifelong reduction in TTR protein after a single dose.

ATTR Amyloidosis with Cardiomyopathy ("ATTR-CM"):

The pivotal Phase 3 MAGNITUDE trial is a randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of NTLA-2001 in adults with ATTR-CM. The primary endpoint of the study is a composite of cardiovascular ("CV")-related mortality and events. Patients will be randomized 2:1 NTLA-2001:placebo, with a single 55 mg infusion of NTLA-2001 administered. In March 2024, the first patients in the U.S. and globally were dosed. The trial is currently enrolling and continues to track ahead of our target enrollment projections. During the second quarter, we received approval for our application under the new European Union Clinical Trials Regulation, which enables the Phase 3 trial to proceed in Denmark, Germany, France, Italy, Spain and Sweden.

Hereditary ATTR Amyloidosis with Polyneuropathy ("ATTRv-PN"):

In November 2024, we announced that the U.S. Food and Drug Administration ("FDA") has cleared our nex-z Investigational New Drug ("IND") application to initiate the MAGNITUDE-2 pivotal Phase 3 trial for ATTRv-PN. MAGNITUDE-2 is an international, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of nex-z in 50 adults with ATTRv-PN. Patients will be randomized 1:1 to receive a single 55 mg infusion of nex-z or placebo. Patients randomized to the placebo arm will be eligible for optional crossover to receive nex-z. The primary endpoints are the change from baseline in modified Neuropathy Impairment Score +7 (mNIS+7) at month 18 and serum TTR at day 29. The mNIS+7 scale is a validated measure specifically designed to assess and quantify polyneuropathy impairment, including muscle weakness, muscle stretch

reflexes, sensory loss and autonomic impairment. We expect to initiate patient enrollment in the MAGNITUDE-2 study at ex-U.S. sites by year-end.

We will be presenting new data from the ongoing Phase 1 study in ATTR-CM patients at the 2024 American Heart Association ("AHA") Scientific Sessions in November. The presentation will include safety, reduction in serum TTR and biomarkers of disease progression and functional capacity data in patients with ATTR-CM.

NTLA-2001 is the subject of a co-development and co-promotion ("Co/Co") arrangement with Regeneron Pharmaceuticals, Inc. ("Regeneron"), ATTR (the "ATTR Co/Co"), for which we are the clinical and commercial lead party and Regeneron is the participating party. Regeneron shares in approximately 25% of worldwide development costs and commercial profits for the ATTR program. For more information regarding our collaboration with Regeneron, see Note 7, "Collaborations and Other Arrangements" of our condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q.

Hereditary Angioedema ("HAE") Program

NTLA-2002 is a wholly owned, investigational *in vivo* CRISPR-based therapy designed to knock out the *kallikrein B1 ("KLKB1")* gene in the liver, with the goal of lifelong control of HAE attacks after a single dose.

In October 2024, we announced the initiation of the HAELO Phase 3 study of NTLA-2002. HAELO is a global, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of NTLA-2002 in 60 adults with Type I or Type II HAE. Patients will be randomized 2:1 to receive a single 50 mg infusion of NTLA-2002 or placebo. Patients randomized to the placebo arm will be eligible for optional crossover to NTLA-2002 at week 28. The primary endpoint is the change in number of HAE attacks from week 5 through week 28. We are actively screening patients in the HAELO Phase 3 study and plan to submit a biologics license application ("BLA") or comparable marketing application in 2026.

Our Phase 1/2 trial of NTLA-2002 evaluated safety, tolerability, activity, pharmacokinetics, and pharmacodynamics. The Phase 1 portion of the study was an open-label, single-ascending dose design. Two dose levels of NTLA-2002 were identified from Phase 1 for further evaluation in the Phase 2, randomized, double-blind, placebo-controlled portion of the study.

In January 2024, we announced that enrollment and dosing was completed in the Phase 2 portion of the study. In August 2024, we announced positive topline results from the Phase 2 study of NTLA-2002 in patients with HAE. The clinical trial met its primary efficacy and all secondary endpoints in the 16-week primary observation period, with a single 25 mg or 50 mg dose leading to deep reductions in attacks. No new safety findings were observed. We selected the 50 mg dose for further evaluation in the global pivotal Phase 3 study based upon the greater number of patients with complete attack elimination and greater kallikrein protein reduction compared to the 25 mg dose observed in the Phase 2 study, which is consistent with the previously reported Phase 1 results.

In June 2024, we presented positive long-term data from the ongoing Phase 1 study. Eight of 10 patients remained completely attack-free following the 16-week primary observation period. These patients have experienced ongoing attack-free durations of greater than 18 months after a single-dose treatment, with the longest ongoing individual attack-free duration reaching over 26 months. Across all patients, NTLA-2002 led to a 98% mean reduction in monthly HAE attack rate compared to baseline. Consistent with previously reported results, NTLA-2002 was well-tolerated, and the majority of adverse events were mild in severity through the latest follow-up. These interim data were presented at the European Academy of Allergy and Clinical Immunology ("EAACI") Congress 2024 in Valencia, Spain.

In August 2024, we also announced the successful completion of an end-of-Phase 2 meeting with the FDA supporting our Phase 3 plans for NTLA-2002.

In October 2024, we presented positive Phase 2 data from the ongoing Phase 1/2 study, with results continuing to support the potential of NTLA-2002 to be a functional cure for HAE. Eight of 11 patients in the 50 mg arm ceased having any attacks during the 16-week primary observation period after a single dose of NTLA-2002. These eight patients continue to be attack-free through the latest follow-up and no subsequent treatment has been required. NTLA-2002 was well tolerated. The most frequent adverse events ("AEs") were headache, fatigue and nasopharyngitis. There have been no serious AEs, and all AEs were either Grade 1 or 2. These interim data were published in The New England Journal of Medicine and presented at the 2024 American College of Allergy, Asthma & Immunology ("ACAAI") Scientific Meeting in Boston, Massachusetts.

Alpha-1 Antitrypsin Deficiency ("AATD") Program

NTLA-3001 is a first-in-class CRISPR-mediated *in vivo* targeted gene insertion development candidate for the treatment of AATD-associated lung disease and our first wholly owned gene insertion program. It is designed to precisely insert the wild-type *SERPINA1* gene, which encodes the alpha-1 antitrypsin ("AAT") protein, with the potential to restore permanent expression of fully functional AAT protein to normal levels after a single dose.

In July 2024, we announced the authorization of our Clinical Trial Application by the United Kingdom's Medicines and Healthcare products Regulatory Agency ("MHRA") to initiate a first-in-human study of NTLA-3001. We expect to dose the first patient in the Phase 1/2 study of NTLA-3001 by year-end. The Phase 1/2 study will be a two-part, open-label, multi-center study with up to 30 patients to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of NTLA-3001.

In Vivo *Research Programs*

In June 2024, we presented positive clinical proof-of-concept data that redosing with CRISPR, utilizing our proprietary non-viral, LNP-based delivery platform, enabled an additive pharmacodynamic effect. In the three patients who previously received the lowest dose of 0.1 mg/kg in the Phase 1 dose-escalation study of NTLA-2001, follow-on dosing with a 55 mg dose of NTLA-2001 led to a deeper protein reduction. Median reduction in serum TTR was 90% at day 28 after redosing. The corresponding reduction from original baseline levels was a 95% median reduction in serum TTR. NTLA-2001 was generally well tolerated across all patients after receiving the follow-on dose. While redosing is not planned for the NTLA-2001 program in ATTR amyloidosis, a redosing option could be an important advantage of our LNP-based delivery platform for future investigational therapies where a target additive effect is desired. These data were presented at the Peripheral Nerve Society ("PNS") Annual Meeting in Montreal, Canada.

We are expanding the range of diseases that can be targeted with our CRISPR-based technologies by deploying new editing and delivery innovations. This includes advancing gene editing programs in five different tissues outside the liver, either independently or in collaboration with partners. These research and preclinical programs are targeting diseases that originate in the bone marrow, brain, muscle, lung and eye which, if successful, could dramatically expand the opportunities for CRISPR-based treatments.

Ex Vivo *Programs*

We are advancing multiple programs, wholly owned and in collaboration with partners, utilizing our allogeneic platform for the treatment of immuno-oncology and autoimmune diseases. Our proprietary allogeneic cell engineering platform avoids both T cell- and natural killer ("NK") cell-mediated rejection in preclinical models, a key unsolved challenge with other investigational allogeneic approaches. Cell therapies engineered with our allogeneic platform, combined with edits to enhance cell function, offer a new approach to target both hematological and solid tumors.

Collaborations and Other Arrangements

To accelerate the development and commercialization of CRISPR/Cas9-based products in multiple therapeutic areas, we have formed, and intend to seek other opportunities to form, strategic alliances with collaborators who can augment our leadership in CRISPR/Cas9 therapeutic development. We have existing collaboration agreements with Regeneron, AvenCell Therapeutics, Inc. ("AvenCell"), SparingVision SAS ("SparingVision"), Kyverna Therapeutics, Inc. ("Kyverna"), ONK Therapeutics, Ltd ("ONK") and ReCode Therapeutics, Inc. ("ReCode"). See Note 7, "Collaborations and Other Arrangements" of our condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q for additional information related to the terms of the agreements between us and our collaborators.

Financial Overview

Collaboration Revenue

Our revenue consists of collaboration revenue, including amounts recognized related to upfront technology access payments for licenses, technology access fees, research materials shipped, research funding and milestone payments earned under our license and collaboration agreements.

Research and Development

Research and development expenses consist of expenses incurred in performing research and development activities, such as compensation and benefits, which includes stock-based compensation, for full-time research and development employees, allocated facility-related expenses, overhead expenses, license and milestone fees, contract research, development and manufacturing services, clinical trial costs and other related costs.

General and Administrative

General and administrative expenses consist primarily of compensation and benefits, including stock-based compensation, for our executive, finance, legal, human resources, business development and support functions. Also included in general and administrative expenses are allocated facility-related costs not otherwise included in research and development expenses, travel expenses and professional fees for auditing, tax and legal services, including IP-related legal services, and other consulting fees and expenses.

Other Income (Expense), Net

During the three and nine months ended September 30, 2024, other income (expense), net consists of interest income earned on our cash, cash equivalents, restricted cash equivalents and marketable securities and change in the fair value of our investments. During the three months ended September 30, 2023, other income (expense), net consisted of interest income earned on our cash, cash equivalents, restricted cash equivalents and marketable securities and loss from our equity method investment. During the nine months ended September 30, 2023, other income (expense), net consisted of interest income earned on our cash, cash equivalents, restricted cash equivalents and marketable securities, loss from our equity method investment and change in fair value of contingent consideration.

Results of Operations

The following discussion of the financial condition and results of operations should be read in conjunction with the accompanying condensed consolidated financial statements and the related footnotes thereto.

Comparison of Three Months Ended September 30, 2024 and 2023

The following table summarizes our results of operations:

	Three Months Ended September 30,		Period-to-Period Change
	2024	2023	
	(In thousands)		
Collaboration revenue	$ 9,111	$ 11,992	$ (2,881)
Operating expenses:			
Research and development	123,380	113,696	9,684
General and administrative	30,501	29,403	1,098
Total operating expenses	153,881	143,099	10,782
Operating loss	(144,770)	(131,107)	(13,663)
Other income (expense), net:			
Interest income	12,122	12,740	(618)
Change in fair value of investments, net	(3,064)	-	(3,064)
Loss from equity method investment	-	(3,857)	3,857
Total other income, net	9,058	8,883	175
Net loss	$ (135,712)	$ (122,224)	$ (13,488)

Collaboration Revenue

Collaboration revenue decreased by $2.9 million during the three months ended September 30, 2024, as compared to the three months ended September 30, 2023. The decrease in collaboration revenue is primarily due to a reduction in revenue under the AvenCell license and collaboration agreement (the “AvenCell LCA”).

Research and Development

Research and development expenses increased by $9.7 million during the three months ended September 30, 2024, as compared to the three months ended September 30, 2023.

The following table summarizes our research and development expenses, together with the changes in those items in dollars and the respective percentages of change:

	Three Months Ended September 30,		Period-to-Period Change	Percent Change
	2024	2023		
	(In thousands)			
External development expenses by program:				
NTLA-2001	$ 22,842	$ 16,404	$ 6,438	39%
NTLA-2002	11,656	4,798	6,858	143%
NTLA-3001	1,766	8,563	(6,797)	-79%
Unallocated research and development expenses:				
Employee-related expenses	29,666	32,317	(2,651)	-8%
Research materials and contracted services	17,922	16,084	1,838	11%
Facility-related expenses	14,206	13,168	1,038	8%
Stock-based compensation	24,224	21,235	2,989	14%
Other	1,098	1,127	(29)	-3%
Total research and development expenses	$ 123,380	$ 113,696	$ 9,684	9%

The increase in research and development expenses for the three months ended September 30, 2024 compared to the three months ended September 30, 2023 was primarily attributable to:

- a $6.4 million increase in external costs related to the development of NTLA-2001, our lead product candidate, primarily due to an increase in spend on contracted services, offset in part by a decrease in drug components;
- a $6.9 million increase in external costs related to the development of NTLA-2002, primarily due to an increase in spend on drug components and contracted services;
- a $6.8 million decrease in external costs related to the development of NTLA-3001, primarily due to a decrease in spend on drug components and contracted services;
- a $2.7 million decrease in employee-related expenses driven by a workforce reduction in January 2024;
- a $1.8 million increase in research materials and contracted services primarily driven by an increase in spend on drug components, offset in part by a decrease in contracted services and internal research and development spend;
- a $1.0 million increase in facility-related expenses primarily related to depreciation, facilities maintenance costs, technology expense allocated to research and development, and rent; and
- a $3.0 million increase in stock-based compensation.

General and Administrative

General and administrative expenses increased by $1.1 million during the three months ended September 30, 2024, as compared to the three months ended September 30, 2023. This increase was primarily related to an increase in stock-based compensation of $1.3 million.

Other Income, Net

The increase in other income, net of $0.2 million is primarily related to a $3.9 million change related to our equity method loss recorded in the third quarter of 2023, offset in part by $3.1 million in expense due to the change in fair value of our investment in Kyverna and a $0.6 million decrease in interest income.

Comparison of Nine Months Ended September 30, 2024 and 2023

The following table summarizes our results of operations:

	Nine Months Ended September 30, 2024	2023	Period-to-Period Change
	(In thousands)		
Collaboration revenue	$ 45,003	$ 38,192	$ 6,811
Operating expenses:			
Research and development	349,434	326,088	23,346
General and administrative	93,385	87,503	5,882
Total operating expenses	442,819	413,591	29,228
Operating loss	(397,816)	(375,399)	(22,417)
Other income (expense), net:			
Interest income	37,176	37,373	(197)
Change in fair value of investments, net	(29,483)	-	(29,483)
Loss from equity method investment	-	(10,905)	10,905
Change in fair value of contingent consideration	-	(100)	100
Total other income, net	7,693	26,368	(18,675)
Net loss	$ (390,123)	$ (349,031)	$ (41,092)

Collaboration Revenue

Collaboration revenue increased by $6.8 million to $45.0 million during the nine months ended September 30, 2024, as compared to $38.2 million during the nine months ended September 30, 2023. The increase in collaboration revenue during the nine months ended September 30, 2024 is primarily due to the recognition of $21.0 million of previously eliminated intra-entity profit under the AvenCell LCA, offset in part by a $12.4 million reduction in revenue related to the AvenCell LCA. Refer to Note 7 to our condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q for further details.

Research and Development

Research and development expenses increased by $23.3 million to $349.4 million during the nine months ended September 30, 2024, as compared to $326.1 million during the nine months ended September 30, 2023.

The following table summarizes our research and development expenses, together with the changes in those items in dollars and the respective percentages of change:

	Nine Months Ended September 30, 2024	2023	Period-to-Period Change	Percent Change
	(In thousands)			
External development expenses by program:				
NTLA-2001	$ 51,206	$ 39,523	$ 11,683	30%
NTLA-2002	31,125	16,408	14,717	90%
NTLA-3001	7,005	16,724	(9,719)	-58%
Unallocated research and development expenses:				
Employee-related expenses	98,184	103,437	(5,253)	-5%
Research materials and contracted services	46,930	46,003	927	2%
Rewrite research milestone	-	874	(874)	-100%
Facility-related expenses	42,175	38,891	3,284	8%
Stock-based compensation	69,824	60,517	9,307	15%
Other	2,985	3,711	(726)	-20%
Total research and development expenses	$ 349,434	$ 326,088	$ 23,346	7%

The increase in research and development expenses for the nine months ended September 30, 2024 compared to the nine months ended September 30, 2023 was primarily attributable to:

- an $11.7 million increase in external costs related to the development of NTLA-2001, our lead product candidate, primarily due to an increase in spend on contracted services and consulting fees, offset in part by a decrease in drug components;

- a $14.7 million increase in external costs related to the development of NTLA-2002, primarily due to an increase in spend on drug components and contracted services;
- a $9.7 million decrease in external costs related to NTLA-3001, primarily related to a decrease in spend on drug components and internal research costs, offset in part by an increase in spend on contracted services;
- a $5.3 million decrease in employee-related expenses, primarily driven by a workforce reduction in January 2024;
- a $0.9 million increase in research materials and contracted services primarily driven by an increase in drug component spend, offset in part by a decrease in internal R&D expenses;
- a $3.3 million increase in facility-related expenses primarily related to depreciation, facility maintenance costs, technology expense allocated to research and development, and rent; and
- a $9.3 million increase in stock-based compensation.

General and Administrative

General and administrative expenses increased by $5.9 million to $93.4 million during the nine months ended September 30, 2024, compared to $87.5 million during the nine months ended September 30, 2023. This increase was primarily related to an increase in stock-based compensation of $6.3 million.

Other Income, Net

The decrease in other income, net of $18.7 million is primarily related to $29.5 million in expense due to the change in fair value of our investments in Kyverna and AvenCell and a $0.2 million decrease in interest income, offset in part by a $10.9 million change related to our equity method loss recorded in the nine months ended September 30, 2023.

Liquidity and Capital Resources

Since our inception through September 30, 2024, we have raised an aggregate of $2,758.3 million to fund our operations through our collaboration agreements, our initial public offering and concurrent private placements, follow-on public offerings, at-the-market offerings and the sale of convertible preferred stock.

As of September 30, 2024, we had $944.7 million in cash, cash equivalents and marketable securities.

At-the-Market Offering Programs

2022 Sale Agreement

In March 2022, we entered into an Open Market Sale Agreement (the “2022 Sale Agreement”) with Jefferies LLC (“Jefferies”), under which Jefferies is able to offer and sell, from time to time in “at-the-market” offerings, shares of our common stock having aggregate gross proceeds of up to $400.0 million. In February 2024, we entered into an amendment to the 2022 Sale Agreement (the “2022 Sale Agreement, as amended”) to increase the size of the at-the-market offering program from $400.0 million to $750.0 million. We agreed to pay cash commissions of up to 3.0% of the gross proceeds of sales of common stock under the 2022 Sale Agreement, as amended. Through September 30, 2024 we have issued 14,522,533 shares of our common stock under the 2022 Sale Agreement, as amended.

During the nine months ended September 30, 2024, we issued 7,004,370 shares of our common stock, in a series of sales, at an average price of $25.68 per share, in accordance with the 2022 Sale Agreement, as amended, for aggregate net proceeds of $174.9 million, after payment of cash commissions and approximately $0.2 million related to legal, accounting and other fees in connection with the sales.

As of September 30, 2024, $249.1 million in shares of common stock remain eligible for sale under the 2022 Sale Agreement, as amended.

Funding Requirements

Our primary uses of capital are, and we expect will continue to be, research and development research materials and contracted services, clinical trial costs, compensation and related expenses, laboratory and office facilities, research supplies, legal and regulatory expenses, patent prosecution filing and maintenance costs for our licensed IP, milestone and royalty payments and general overhead costs. During the remainder of 2024, we expect our expenses to increase compared to prior periods in connection with our ongoing activities as we continue to develop our clinical programs and advance additional programs into clinical development.

Because our lead programs are in the clinical stage and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of any future product candidates or whether, or when, we may achieve profitability. Until such time as we can generate substantial product revenues, if ever, we expect to fund our ongoing cash needs through equity financings and collaboration arrangements. We receive cost reimbursements from Regeneron related to our collaboration agreements with them. Additionally, we are eligible to earn milestone payments and royalties, in each case, on a per-product basis under our collaborations with SparingVision, ONK and ReCode, on a per-target basis under our collaboration with Regeneron, and upon achievement of certain events with Kyverna, subject to the provisions of our agreements with each of them. Except for these sources of funding, we will not have any committed external source of liquidity. To the extent that we raise additional capital through the future sale of equity, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing stockholders. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Outlook

Based on our research and development plans and our expectations related to the progress of our programs, we expect that our cash, cash equivalents and marketable securities as of September 30, 2024, as well as research and cost reimbursement funding from our collaboration agreements, will enable us to fund our ongoing operating expenses and capital expenditure requirements into late 2026, excluding any potential milestone payments or extension fees that could be earned and distributed under our collaboration agreements or any strategic use of capital not currently in the base case planning assumptions. We have based this estimate on current assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect.

Our ability to generate revenue and achieve profitability depends significantly on our success in many areas, including: developing our delivery technologies and our CRISPR/Cas9 technology platform; selecting appropriate product candidates to develop; completing research and preclinical and clinical development of selected product candidates; obtaining regulatory approvals and marketing authorizations for product candidates for which we complete clinical trials; developing a sustainable and scalable manufacturing process for product candidates; launching and commercializing product candidates for which we obtain regulatory approvals and marketing authorizations, either directly or with a collaborator or distributor; obtaining market acceptance of our product candidates; addressing any competing technological and market developments; negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter; maintaining good relationships with our collaborators and licensors; maintaining, protecting, and expanding our portfolio of IP rights, including patents, trade secrets, and know-how; and attracting, hiring, and retaining qualified personnel.

Cash Flows

The following is a summary of cash flows:

	Nine Months Ended September 30,	
	2024	2023
	(In thousands)	
Net cash used in operating activities	$ (263,685)	$ (301,032)
Net cash used in investing activities	(25,998)	(77,286)
Net cash provided by financing activities	183,430	23,839

Net cash used in operating activities

Net cash used in operating activities of $263.7 million during the nine months ended September 30, 2024 primarily consists of a net loss of $390.1 million, further reduced by the non-cash recognition of $21.0 million of previously eliminated intra-entity profit recorded within “collaboration revenue” and accretion of investment discounts and premiums of $14.2 million. These decreases are offset in part by stock-based compensation of $114.7 million, $29.5 million in net adjustments to the fair value of our investments in Kyverna and AvenCell, net changes in operating assets and liabilities of $9.8 million and depreciation of $7.7 million.

Net cash used in operating activities of $301.0 million during the nine months ended September 30, 2023 primarily consists of a net loss of $349.0 million, further reduced by changes in operating assets and liabilities of $55.6 million, including the receipt of $12.6 million in payments from our collaboration partners during that period and offset in part by non-cash charges of stock-based compensation of $99.0 million, loss on equity method investment of $17.5 million and depreciation of $6.5 million.

Net cash used in investing activities

During the nine months ended September 30, 2024, we used $26.0 million of net cash in investing activities. The decrease in the nine months ended September 30, 2024 is primarily due to $21.2 million in marketable securities purchased (net of maturities) and $4.8 million in cash for the purchase of property and equipment.

During the nine months ended September 30, 2023 we used cash of $77.3 million in investing activities. The decrease in the nine months ended September 30, 2023 is primarily due to $64.8 million in marketable securities purchased (net of maturities) and $12.5 million in cash for the purchase of property and equipment.

Net cash provided by financing activities

Net cash provided by financing activities of $183.4 million during the nine months ended September 30, 2024 includes $176.9 million in net proceeds from at-the-market offerings, $4.8 million in cash received from the exercise of stock options and $1.7 million in cash received from the issuance of shares through our employee stock purchase plan.

Net cash provided by financing activities of $23.8 million during the nine months ended September 30, 2023 includes $16.2 million in net proceeds from at-the-market offerings, $5.6 million in cash received from the exercise of stock options and $2.1 million in cash received from the issuance of shares through our employee stock purchase plan.

Critical Accounting Policies

Our critical accounting policies require the most significant judgments and estimates in the preparation of our condensed consolidated financial statements. Management has determined that our most critical accounting policies are those relating to revenue recognition, accrued research and development expenses and stock-based compensation. There have been no changes to our critical accounting policies from those which were discussed in our Annual Report for the year ended December 31, 2023.

Recent Accounting Pronouncements

Please read Note 2, “Summary of Significant Accounting Policies,” to our condensed consolidated financial statements included in Part I, Item 1, “Notes to Condensed Consolidated Financial Statements,” of this Quarterly Report on Form 10-Q for a description of recent accounting pronouncements applicable to our business.

Contractual Obligations

There were no material changes to our contractual obligations during the three months ended September 30, 2024. For a complete discussion of our contractual obligations, please refer to our *Management’s Discussion and Analysis of Financial Condition and Results of Operations* in our Annual Report for the year ended December 31, 2023.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of September 30, 2024, we had cash equivalents, restricted cash equivalents and marketable securities of $917.5 million consisting of interest-bearing money market accounts, corporate and financial institution debt securities, U.S. Treasury and other government-backed securities and asset-backed securities. Our primary exposure to market

risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are primarily in marketable securities. Due to the short-term duration of our investment portfolios and the low risk profile of our investments, we do not believe an immediate change of 100 basis points, or one percentage point, would have a material effect on the fair market value of our investment portfolio. Declines in interest rates, however, would reduce future investment income.

We do not have any foreign currency or derivative financial instruments. Inflation generally affects us by increasing our cost of labor and program costs. We do not believe that inflation had a material effect on our results of operations during the nine months ended September 30, 2024.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We have established disclosure controls and procedures designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and is accumulated and communicated to management, including the principal executive officer (our Chief Executive Officer) and principal financial officer (our Chief Financial Officer), to allow timely decisions regarding required disclosure.

Our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, has 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 the end of the period covered by this Quarterly Report on Form 10-Q. Management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of September 30, 2024.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended September 30, 2024 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II - OTHER INFORMATION

Item 1. Legal Proceedings

In the ordinary course of business, we are from time to time involved in lawsuits, claims, investigations, proceedings, and threats of litigation related to intellectual property ("IP"), commercial arrangements and other matters. The outcome of any such legal proceedings, regardless of the merits, is inherently uncertain. In addition, litigation and related matters are costly and may divert the attention of our management and other resources that would otherwise be engaged in other activities. If we were unable to prevail in any such legal proceedings, our business, results of operations, liquidity and financial condition could be adversely affected.

BlueAllele Corp. v. Intellia Therapeutics, Inc.

On July 8, 2024, BlueAllele Corp. ("BlueAllele") filed a complaint alleging infringement by Intellia of various patents in the U.S. District Court for the District of Delaware. Specifically, BlueAllele alleges that our experimentation, basic research, identification, optimization, manufacturing and/or use of bi-directional insertion template technology infringes the asserted patents and seeks, *inter alia*, unspecified compensatory damages and an injunction against the alleged infringing activities. On September 12, 2024, we filed a motion to dismiss the complaint. On October 23, 2024, BlueAllele responded to the motion to dismiss.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. In evaluating us and our business, careful consideration should be given to the following risk factors, in addition to the other information set forth in this Quarterly Report on Form 10-Q, our Annual Report on Form 10-K for the year ended December 31, 2023, and in other documents that we file with the Securities and Exchange Commission ("SEC"). If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks summarized and described below are not intended to be exhaustive and are not the only risks facing us. New risk factors can emerge from time to time, and we cannot predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations.

The risk factors denoted with a "*", if any, are newly added or have been materially updated from our Annual Report on Form 10-K for the year ended December 31, 2023.

Summary of the Material Risks Associated with Our Business

- CRISPR/Cas9 genome editing technology has limited clinical validation and has only recently been approved for human therapeutic use. The approaches we are taking to discover and develop novel therapeutics using CRISPR/Cas9 systems are unproven and may never lead to marketable products. If we are unable to develop viable product candidates, achieve regulatory approval for any such product candidate or market and sell any products, we may never achieve profitability.
- Clinical development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates.
- Results, including data from our preclinical studies and clinical trials, that we announce from time to time, such as the interim data from our ongoing Phase 1 study of NTLA-2001 or Phase 1/2 study of NTLA-2002, are not necessarily predictive of our other ongoing and future preclinical and clinical studies, and they do not guarantee or indicate the likelihood of approval of any potential product candidate by the United States Food and Drug Administration ("FDA") or any other regulatory agency. If we cannot replicate the positive results from any of our preclinical or clinical studies, we may be unable to successfully develop, obtain regulatory approval for and commercialize any potential product candidate.
- Negative public opinion and increased regulatory scrutiny of CRISPR/Cas9 use, genome editing or gene therapy generally may damage public perception of the safety of any product candidates that we develop and adversely affect our ability to conduct our business or obtain regulatory approvals for such product candidates.
- Even if we obtain regulatory approval of any product candidates, such candidates may not gain market acceptance among physicians, patients, hospitals, third party payors and others in the medical community.

•Under our license agreement with Caribou Biosciences, Inc. (“Caribou”), we sublicense a patent family from the Regents of the University of California and the University of Vienna that is co-owned by Dr. Emmanuel Charpentier (collectively, “UC/Vienna/Charpentier”). The outcome of ongoing legal proceedings, as well as potential future proceedings, related to this patent family may affect our rights under certain intellectual property sublicensed under our license agreement with Caribou.

•We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products or product candidates, or asserting and defending our intellectual property rights that protect our products and technologies.

•Third parties may have patent rights and other intellectual property rights that cover our product candidates, and we may be unable to avoid, obtain or invalidate patent rights owned by third parties that are necessary to develop, manufacture or commercialize our product candidates in one or more jurisdictions.

•Our ability to generate revenue from product sales and become profitable is dependent on the success of our application of CRISPR/Cas9 technology for human therapeutic use, which is at a clinical stage of development and will require significant additional discovery efforts, preclinical testing and clinical studies and manufacturing capabilities, as well as applicable regulatory guidance regarding preclinical testing and clinical studies from the FDA and other similar regulatory authorities, before we can seek regulatory approval and begin commercial sales of any potential product candidates.

•We have incurred net losses in each period since our inception, anticipate that we will continue to incur net losses in the future and may never achieve profitability.

•*In vivo* genome editing products and *ex vivo* engineered cell therapies based on CRISPR/Cas9 genome editing technology are novel and may be complex and difficult to manufacture. We could experience manufacturing problems or regulatory requirements that result in delays in the development, approval or commercialization of our product candidates or otherwise harm our business.

•If we experience delays or difficulties in the enrollment of patients in clinical trials, our ability to complete clinical trials or our receipt of necessary regulatory approvals could be delayed or prevented.

•Our technological advancements and any potential for revenue may be derived in part from our collaborations, including, for example, with Regeneron Pharmaceuticals, Inc. (“Regeneron”), and if the collaboration or co-development agreements related to a material collaboration were to be terminated or materially altered in an adverse manner, our business, financial condition, results of operations and prospects may be harmed.

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

•We face significant competition in an environment of rapid technological change. The possibility that our competitors may achieve regulatory approval before we do or develop therapies that are more advanced or effective than ours may harm our business and financial condition or our ability to successfully market or commercialize our product candidates.

•The price of our common stock historically has been volatile, which may affect the price at which you could sell any shares of our common stock.

Risks Related to Our Business

Risks Related to Preclinical and Clinical Development

CRISPR/Cas9 genome editing technology has only recently been clinically validated for human therapeutic use. The approaches we are taking to discover and develop novel therapeutics using CRISPR/Cas9 systems are unproven and may never lead to marketable products. If we are unable to develop viable product candidates, achieve regulatory approval for any such product candidate or market and sell any product candidates, we may never achieve profitability.

We are focused on developing curative medicines utilizing CRISPR/Cas9 genome editing technology, including *in vivo* therapies and *ex vivo* engineered cell therapies. Although there have been significant advances in recent years in the fields of gene therapy and genome editing, *in vivo* CRISPR-based genome editing technologies are relatively new and their therapeutic utility is largely unproven. Our approach to developing therapies centers on using CRISPR/Cas9 technology to alter, introduce or remove genetic

information *in vivo* to treat various disorders, or to engineer human cells *ex vivo* to create therapeutic cells that can be introduced into the human body to address the underlying disease.

Successful development of products by us will require solving a number of issues, including developing or obtaining technologies to safely deliver a therapeutic agent into target cells within the human body or engineer human cells while outside of the body such that the modified cells can have a therapeutic effect when delivered to the patient, optimizing the efficacy and specificity of such products, and ensuring and demonstrating the therapeutic selectivity, efficacy, potency, purity and safety of such products. There can be no assurance we will be successful in solving any or all of these issues. With regards to CRISPR/Cas9-based therapies specifically, we are in clinical-stage development for NTLA-2001, NTLA-2002 and NTLA-3001, and advancing towards clinical testing for our other *in vivo* and *ex vivo* product candidates. Although one CRISPR/Cas9-edited *ex vivo* therapy has been recently approved in the United States ("U.S.") and European Union ("EU"), no genome editing *in vivo* therapy has been approved in the U.S., EU countries or other key jurisdictions, and the potential to successfully obtain approval for any of our CRISPR/Cas9 product candidates remains unproven.

Our future success also is highly dependent on the successful development of CRISPR-based genome editing technologies, cellular delivery methods and therapeutic applications for the indications on which we have focused our ongoing research and development efforts. We may decide to alter or abandon these programs as new data become available and we gain experience in developing CRISPR/Cas9-based therapeutics. We cannot be sure that our CRISPR/Cas9 efforts and technologies will yield satisfactory products that are safe and effective, sufficiently pure or potent, manufacturable, scalable or profitable in our selected indications or any other indication we pursue. We cannot guarantee that progress or success in developing any particular CRISPR/Cas9-based therapeutic product will translate to other CRISPR/Cas9-based products.

Public perception and related media coverage of potential therapy-related efficacy or safety issues, including adoption of new therapeutics or novel approaches to treatment, as well as ethical concerns related specifically to genome editing and CRISPR/Cas9, may adversely influence the willingness of subjects to participate in clinical trials, or if any therapeutic is approved, of physicians and patients to accept these novel and personalized treatments. Physicians, healthcare providers and third party payors often are slow to adopt new products, technologies and treatment practices, particularly those that may also require additional upfront costs and training. Physicians may not be willing to undergo training to adopt these novel and potentially personalized therapies, may decide the particular therapy is too complex or potentially risky to adopt without appropriate training, and may choose not to administer the therapy. Further, due to health conditions, genetic profile or other reasons, certain patients may not be candidates for the therapies. In addition, responses by federal and state agencies, congressional committees and foreign governments to negative public perception, ethical concerns or financial considerations may result in new legislation, regulations, or medical standards that could limit our ability to develop or commercialize any product candidates, obtain or maintain regulatory approval or otherwise achieve profitability. New government requirements may be established that could delay or prevent regulatory approval of our product candidates under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be. Based on these and other factors, healthcare providers and payors may decide that the benefits of these new therapies do not or will not outweigh their costs.

Clinical development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates.*

All of our programs are still in the discovery, preclinical or clinical stage. Our current and future product candidates will require preclinical and clinical activities and studies, regulatory review and approval in each jurisdiction in which we intend to market the products, substantial investment, establishing manufacturing capabilities, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. Before obtaining marketing approval from regulatory authorities for the sale of a product candidate, we must conduct extensive clinical trials to demonstrate the safety, purity, potency and efficacy of the product in humans. It is impossible to predict when or if any of our programs will prove effective and safe in humans or will receive regulatory approval. Preclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. We may be unable to establish clinical endpoints that regulatory authorities consider clinically meaningful, and a clinical trial can fail at any stage. The outcome of preclinical testing and clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain approval of their products.

Successful completion of clinical trials is a prerequisite to submitting a Biologics License Application ("BLA") to the FDA, and similar applications to comparable foreign regulatory authorities, for each product candidate and, consequently, the ultimate approval and commercial marketing of any product candidates. We do not know whether any of our clinical trials will begin or be completed on schedule, if at all. In addition, the regulatory requirements for later phase clinical trials, such as pivotal trials, are generally more stringent than earlier phase clinical trials, such as Phase 1 trials. We may not meet the requirements of regulatory authorities, such as the FDA, for initiating later phase clinical trials for our product candidates, which could delay the development of our product candidates, including the submission of a BLA or comparable marketing application.

Because these are new therapeutic approaches, discovering, developing, manufacturing and commercializing our product candidates may subject us to a number of challenges or delays in completing our preclinical studies and initiating or completing clinical trials. We also may experience numerous unforeseen events during, or as a result of, any current or future clinical trials that we conduct, which could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- challenges in obtaining regulatory authorization or approval to conduct clinical trials in the U.S. from the FDA through an investigational new drug ("IND") application or from other regulatory agencies outside the U.S., such as the United Kingdom ("U.K.") Medicines and Healthcare products Regulatory Agency ("MHRA") or the European Medicines Agency ("EMA"), through corresponding applications, such as a clinical trial application, a clinical trial notification or a clinical trial exemption, because these agencies have very limited or no experience with the clinical development of CRISPR/Cas9-based therapeutics, particularly *in vivo* therapeutics, which may require additional significant testing or data compared to more traditional therapies or otherwise delay the development of our product candidates;
- successfully developing processes for the safe administration of these product candidates, including long-term follow-up for patients who receive treatment with any of our product candidates;
- regulators, institutional review boards ("IRBs") or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial;
- inability to reach, or delays in reaching, agreement on acceptable terms with trial sites and contract research organizations ("CROs");
- clinical trials of any product candidates may fail to show safety or efficacy, or could produce negative or inconclusive results, which could result in having to conduct additional preclinical studies or clinical trials or terminating the product development programs;
- we may not be able to initiate or complete clinical trials of a product candidate if the required number of subjects is larger than we anticipated, the number of subjects willing to enroll is smaller than required, the pace of enrollment is slower than anticipated, or subjects drop out or fail to return for post-treatment follow-up at a higher rate than we anticipated;
- we may need to educate medical personnel, including clinical investigators, and patients regarding the potential benefits and side effect profile of each of our product candidates;
- regulatory agencies may require us to amend our INDs or equivalent regulatory filings, modify the design of our clinical trials or perform more extensive or lengthier preclinical or clinical testing compared to existing therapeutic modalities, any of which may delay the initiation or progression of any of our clinical trials;
- animal models may not exist, or available animal models may be inadequate, for some of the human diseases we choose to pursue in our programs, or the preclinical studies we perform as part of our programs;
- our third party contractors may fail to comply with regulatory requirements or meet their performance obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of preclinical studies and clinical trials of any product candidates may be greater than we anticipate;

- the supply or quality of our product candidates or other materials necessary to conduct preclinical studies and clinical trials of our product candidates may be insufficient or inadequate, or not available in a reasonable timeframe, and any transfer of manufacturing activities may require unforeseen manufacturing or formulation changes;
- we may face challenges in sourcing preclinical, clinical and, if approved, commercial supplies for the materials used to manufacture and process our product candidates, which may include importing or exporting materials between different jurisdictions;
- our product candidates may have undesirable side effects or other unexpected characteristics, such as effects or characteristics resulting from their biodistribution or mechanism of action, causing us or our investigators, regulators, IRBs or ethics committees to suspend or terminate the trials, or reports may arise from preclinical or clinical testing of other gene therapies or genome editing-based therapies that raise safety or efficacy concerns about our product candidates;
- the FDA or other regulatory authorities may require us to submit additional data, such as long-term toxicology studies, or impose other requirements, including submitting preclinical data earlier in clinical development compared to existing therapeutic modalities or requiring amendments to our regulatory filings, before permitting us to initiate or rely on a clinical trial;
- we may face challenges in establishing sales and marketing capabilities in anticipation of, and after obtaining, any regulatory approval to gain market authorization;
- the FDA or other regulatory authorities may revise the requirements for authorizing our clinical trials or approving our product candidates, or their interpretation of the authorization or approval requirements may not be what we anticipate or require us to adopt Risk Evaluation and Mitigation Strategy ("REMS") as a condition of approval; and
- we may not ultimately obtain regulatory approval for a BLA, or corresponding applications outside the U.S., such as a marketing authorization application in the U.K. and other similar regulatory authorities, such as the EMA, which may have very limited or no experience with the clinical development of CRISPR/Cas9-based therapeutics, particularly *in vivo* therapeutics.

We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, the relevant ethics committee or the FDA or other relevant regulatory authorities, or if the Data Monitoring Committee ("DMC") for such trial recommends such suspension or termination. Such authorities may impose or recommend such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities, resulting in the imposition of a clinical hold, manufacturing or quality control issues, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product or treatment, failure to establish or achieve clinically meaningful trial endpoints, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also lead to a delay in submitting a BLA or comparable marketing application or ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials.

Additionally, because our *in vivo* technology potentially involves genome editing across multiple cell and tissue types, we are subject to many of the challenges and risks that other genome editing therapeutics and gene therapies face, including:

- regulatory guidance regarding the requirements governing gene and genome editing therapy products have changed and may continue to change in the future, including, e.g., the finalized guidance document titled "Human Gene Therapy Products Incorporating Human Genome Editing" that the FDA issued in January 2024;
- to date, only a limited number of products that involve *in vivo* gene transfer have been approved globally;
- improper modulation of a gene sequence, including unintended editing events, insertion of a sequence into certain locations in a patient's chromosome or other effects related to the biodistribution of our product candidates, could lead to cancer, other aberrantly functioning cells or other diseases, including death;
- transient expression of the Cas9 protein or other genome editing components of our product candidates could lead to patients having an immunological reaction towards those cells, which could be severe or life-threatening;

- corrective expression of a missing protein in patients' cells could result in the protein being recognized as foreign, and lead to a sustained immunological reaction against the expressed protein or expressing cells, which could be severe or life-threatening; and
- regulatory agencies may require extended follow-up observation periods of patients who receive treatment using genome editing products including, for example, the FDA's recommended 15-year follow-up observation period for these patients, and we will need to adopt such observation periods for our product candidates if required by the relevant regulatory agency, which could vary by country or region.

Further, because our *ex vivo* product candidates involve editing human cells and then delivering modified cells to patients, we are subject to many of the challenges and risks that engineered cell therapies face. For example, patients treated with engineered cell-based gene therapies may experience an allogeneic response leading to allograft rejection and potential local and systemic toxicities, which could be severe or life-threatening.

To date, most human clinical trials utilizing either *in vivo* or *ex vivo* CRISPR-based therapeutics, including our clinical trials for NTLA-2001 for transthyretin ("ATTR") amyloidosis, NTLA-2002 for hereditary angioedema ("HAE") and NTLA-3001 for alpha-1 antitrypsin deficiency ("AATD")-associated lung disease, are still at a clinical stage, with only one *ex vivo* CRISPR-based therapeutic product approved in December 2023 in the U.S. and EU. We have ongoing clinical trials in various countries for NTLA-2001 and NTLA-2002 for patients with ATTR amyloidosis and HAE, respectively. There is no certainty that the FDA or other similar agencies will continue to apply to all our CRISPR/Cas9 product candidates the same regulatory pathway and requirements it is applying to other *in vivo* therapies or *ex vivo* engineered therapeutics.

In addition, if any product candidates encounter safety or efficacy problems, development delays, regulatory issues or other problems, our development plans and business could be significantly harmed. For the reasons described above, among others, regulatory bodies, particularly the FDA, have requested, and may request in the future, additional preclinical studies for genome editing products, such as additional studies related to toxicology, biodistribution or reproductive health, and/or preclinical studies earlier in clinical development compared to other therapeutic modalities. Although the FDA cleared the INDs that we have submitted, it is possible that the FDA may impose requirements that result in a delay of any of our programs, including our submission of a BLA or comparable marketing application, or their regulatory approval. For example, following the March 2023 IND clearance for NTLA-2002, the FDA requested supplemental preclinical data related to the inclusion of female patients of child-bearing potential, which we have since provided to the FDA in advance of the planned Phase 3 study and have received written feedback from the FDA that the data provided support inclusion of female patients of child-bearing potential in the Phase 3 study. If we are unable to complete the required studies satisfactorily, the FDA or other regulatory bodies could require that we exclude certain patient populations from clinical studies, place our clinical studies on hold, or require us to cease further clinical studies or deny approval of such product candidates. Further, competitors that are developing *in vivo* or *ex vivo* products with similar technology may experience problems with their product candidates or programs that could in turn cause us to identify problems with our product candidates and programs, or cause the FDA or other regulatory bodies to impose additional requirements, that could cause us to delay or pause development of our product candidates. Any of these occurrences may harm our ability to identify and develop product candidates, and may harm our business, financial condition, results of operations and prospects significantly.

We may experience manufacturing delays or other issues that prevent us from executing the clinical trials for NTLA-2001, NTLA-2002, NTLA-3001 or our other product candidates on the timeline we expect. Moreover, we cannot guarantee that the FDA, MHRA, the New Zealand Medicines and Medical Devices Safety Authority, or other regulatory authorities will not change their requirements in the future or approve amendments to our INDs or equivalent regulatory filings, including for NTLA-2001, NTLA-2002, NTLA-3001 or our other product candidates on the timeline we expect.

Results, including data from our preclinical and clinical studies, are not necessarily predictive of our other ongoing and future preclinical and clinical studies, and they do not guarantee or indicate the likelihood of approval of any potential product candidate by the FDA or any other regulatory agency. If we cannot replicate positive results from any of our preclinical or clinical activities and studies, we may be unable to successfully develop, obtain regulatory approval for and commercialize any potential product candidate.

From time to time, we may disclose interim data from our clinical trials, such as the interim results of our ongoing Phase 1 study of NTLA-2001 or Phase 1/2 study of NTLA-2002 or planned Phase 1/2 study of NTLA-3001. Interim data from clinical trials that have not been completed 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 or as patients from our clinical trials continue other treatments for their disease. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Consequently, interim data should be viewed with caution until we make the final data and analysis available.

In addition, there is a high failure rate, as well as potential substantial and unanticipated delays, for product candidates progressing through preclinical and clinical studies. Even if we are able to successfully complete our ongoing and future preclinical and clinical activities and studies for any potential product candidate, we may not be able to replicate, or may have to engage in significant efforts and resource and time investments to replicate, any positive results from these or any other studies in any of our future preclinical and clinical trials, and they do not guarantee approval of any potential product candidate by the FDA or any other necessary regulatory authorities in a timely manner or at all. For more information regarding these risks, see also the remainder of this risk factor section.

Negative public opinion and increased regulatory scrutiny of CRISPR/Cas9 use, genome editing or gene therapy generally may damage public perception of the safety of any product candidates that we develop and adversely affect our ability to conduct our business or obtain regulatory approvals for such product candidates.

Gene therapy in general, and genome editing in particular, remain novel technologies, with only a limited number of gene therapy products, and only one *ex vivo* genome editing product, approved to date in the U.S. and EU. Public perception may be influenced by claims that gene therapy or genome editing, including the use of CRISPR/Cas9, is unsafe or unethical, or carries an undue risk of side effects, such as improper modification of a gene sequence in a patient's chromosome that could lead to cancer, and gene therapy or genome editing may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians who specialize in the treatment of diseases targeted by our product candidates prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments with which they are more familiar and for which greater clinical data may be available. In addition, responses by the U.S., state or foreign governments to negative public perception or ethical concerns may result in new legislation or regulations that could limit our ability to develop or commercialize any product candidates, obtain or maintain regulatory approval or otherwise achieve profitability. More restrictive statutory regimes, government regulations or negative public opinion could have an adverse effect on our business, financial condition and results of operations and prospects, and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, certain gene therapy trials led to several well-publicized adverse events, including cases of leukemia and death. Serious adverse events, such as these, in our clinical trials, or other clinical trials involving gene therapy or genome editing products or our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidate. In addition, the use of the technology by third parties in areas that are not being pursued by us, such as for targeting and editing of embryonic cells, could adversely impact public and governmental perceptions regarding the ethics and risks of the CRISPR/Cas9 technology and lead to social or legal changes that could limit our ability to apply the technology to develop human therapies addressing disease. For example, reports of the use of CRISPR/Cas9 in China and Russia to edit embryos *in utero* have generated, and may continue to generate, negative public perception about the use of the technology in humans. Negative public and governmental perception of the technology, or additional governmental regulation of our technologies, could also adversely affect our stock price or our ability to enter into revenue generating collaborations or obtain additional funding from the public markets.

Risks Related to the Industry

Inconclusive results, lack of efficacy, adverse events or additional safety concerns in clinical trials that we or others conduct may impede the regulatory approval process or overall market acceptance of our product candidates.

Therapeutic applications of genome editing technologies, and CRISPR/Cas9 in particular, for both *in vivo* products and *ex vivo* products, are unproven and must undergo rigorous clinical trials and regulatory review before receiving marketing authorization. If the results of our clinical studies or those of any other third parties, including with respect to genome editing technology or engineered cell therapies, are inconclusive or fail to show efficacy or if such clinical trials give rise to safety concerns or adverse events, we may:

- be prevented from, or delayed in, obtaining marketing approval for our product candidates;

•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 the addition of labeling statements, such as warnings or contraindications, or other types of regulatory restrictions or scrutiny;

•be subject to changes in the way the product is administered;

•be required to perform additional clinical studies to support approval or be subject to additional post-marketing testing requirements;

•have regulatory authorities modify or withdraw their legal requirements or written guidance, if any, regarding the applicable regulatory approval pathway or any approval of the product in question, or impose restrictions on its distribution in the form of a modified REMS or similar strategy;

•be sued; or

•experience damage to our reputation.

Additionally, our product candidates could potentially cause other adverse events that have not yet been predicted and the potentially permanent nature of genome editing effects, including CRISPR/Cas9's effects, on genes or novel cell therapies in the organs of the human body may make these adverse events irreversible. The inclusion of critically ill patients in our clinical studies or those of our competitors may result in deaths or other adverse medical events, including those due to other therapies or medications that such patients may be using. Any of these events could prevent us from achieving or maintaining regulatory approval or market acceptance of our product candidates and impair our ability to achieve profitability.

Research and development of biopharmaceutical products is inherently risky. We may not be successful in our efforts to use and enhance our genome editing technology to create a pipeline of product candidates, establish the necessary manufacturing capabilities, obtain regulatory approval and develop commercially successful products, or we may expend our limited resources on programs that do not yield a successful product candidate and fail to capitalize on potential product candidates or diseases that may be more profitable or for which there is a greater likelihood of success. If we fail to develop product candidates, our commercial opportunity, if any, will be limited.

We are at a clinical stage of development and our technology and approach has not yet led, and may never lead, to the approval or commercialization of any of our product candidates, including NTLA-2001 for ATTR amyloidosis, NTLA-2002 for HAE, or NTLA-3001 for AATD, or to our other product candidates being deemed appropriate for clinical development and ultimately approval by a regulatory agency. Even if we are successful in building our pipeline of product candidates, completing clinical development, establishing the necessary manufacturing processes and capabilities, obtaining regulatory approvals and commercializing product candidates will require substantial additional funding and are subject to the risks of failure inherent in therapeutic product development. Investment in biopharmaceutical product development involves significant risk that any potential product candidate will fail to demonstrate acceptable safety and efficacy profiles, gain regulatory approval, or become commercially viable.

We cannot provide any assurance that we will be able to successfully advance any of our product candidates, including NTLA-2001, NTLA-2002, NTLA-3001 or product candidates developed through our collaborations, through the entire research and development process. Any of our other programs may show promise, yet fail to yield product candidates for clinical development or commercialization for many reasons. For more information regarding these risks, see the above risk factor section entitled "Risks Related to Preclinical and Clinical Development."

Even if we obtain regulatory approval of any product candidates, such candidates may not gain market acceptance among physicians, patients, hospitals, third party payors and others in the medical community.

The use of the CRISPR/Cas9 system to create genome editing-based therapies is a recent development and may not become broadly accepted by patients, healthcare providers, third party payors and other stakeholders. A variety of factors will influence whether our product candidates are accepted in the market, including, for example:

•the clinical indications for which our product candidates are approved;

•the potential and perceived advantages of our product candidates over alternative treatments;

- the incidence and severity of any side effects, including any unintended deoxyribonucleic acid ("DNA") changes;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA or other regulatory authorities;
- the timing of market introduction of our product candidates;
- availability or existence of competitive products;
- the cost of treatment in relation to alternative treatments;
- the amount of upfront costs or training required for healthcare providers to administer our product candidates;
- the availability of adequate coverage, reimbursement and pricing by government authorities and other third party payors;
- patients' ability to access healthcare providers capable of delivering our product candidates;
- patients' willingness and ability to pay out-of-pocket in the absence of coverage and reimbursement by government authorities and other third party payors;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies;
- any restrictions on the use of our product candidates together with other medications;
- interactions of our product candidates with other medicines patients are taking;
- potential adverse events for any products developed, or negative interactions with regulatory agencies, by us or others in the gene therapy and genome editing fields; and
- the effectiveness of our sales and marketing efforts and distribution support.

Even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete. In addition, adverse publicity due to the ethical and social controversies surrounding the therapeutic *in vivo* use of CRISPR/Cas9, genome edited modified cells, or other therapeutics mediums, such as viral vectors that we may use in our clinical trials may limit market acceptance of our product candidates. If our product candidates are approved but fail to achieve market acceptance among physicians, patients, hospitals, third party payors or others in the medical community, we will not be able to generate significant revenue. Our efforts to educate the healthcare providers, patients and third party payors about our products may require significant resources and may never be successful.

Risks Related to Intellectual Property

Risks Related to Third Party and Licensed Intellectual Property

Third party claims of intellectual property infringement against us, our licensors or our collaborators may prevent or delay our product discovery and development efforts.

Our commercial success depends in part on our avoiding infringement of the valid patents and proprietary rights of third parties.

Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are developing our product candidates and in areas potentially related to components and methods we use or may use in our research and development efforts. As industry, government, academia and other biotechnology and pharmaceutical research expands and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Our development candidates are complex and may include multiple components such as Cas9 protein or messenger ribonucleic acid encoding Cas9 protein, guide ribonucleic acids ("gRNAs"), targeting molecules, or formulation components such as lipids. We cannot guarantee that any of these components of our technology, processes, future product candidates or the use of such product candidates do not infringe third party patents. It is also possible that we have failed to identify relevant third party patents or applications. Because patent rights are granted jurisdiction-by-jurisdiction, our freedom

to practice certain technologies, including our ability to research, develop and commercialize our product candidates, may differ by country.

Third parties may assert that we infringe their patents or that we are otherwise employing their proprietary technology without authorization, and may sue us. There may be third party patents with claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover product candidates we discover and develop. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies or the manufacture, use or sale of our product candidates or products that we develop infringes these patents. If a court of competent jurisdiction were to hold that we infringed such patents, the holders of any such patents may be able to block our ability to commercialize the applicable product candidate or products unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be held invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing, manufacturing or importing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing one or more of our product candidates or products that we develop, force us to redesign our infringing products or force us to cease some or all of our business operations, any of which could materially harm our business and could prevent us from further developing and commercializing such products or future product candidates, thereby causing us significant harm. If we are unable to obtain a necessary license to a third party patent on commercially reasonable terms, our ability to commercialize our product candidates or products that we develop may be impaired or delayed, which could in turn significantly harm our business. In addition, we may be obligated to defend and/or indemnify our existing or potential collaborators, clinical investigators, contract manufacturing organizations ("CMOs"), CROs, consultants or vendors if a third party asserts similar infringement claims against them based on use of our technologies or the manufacture, use or sale of our product candidates or products that we develop, including product candidates or products developed with our collaborators. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. Even if we are not found liable for infringing or misappropriating the intellectual property of a third party, such claims could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

Third parties may seek to claim intellectual property rights that encompass or overlap with intellectual property that we own or license from them or others. Legal proceedings may be initiated to determine the scope and ownership of these rights, and could result in our loss of rights, including injunctions or other equitable relief that could effectively block our ability to further develop and commercialize our product candidates or products that we develop, including product candidates or products developed with our collaborators. For example, through a license agreement between Caribou Biosciences, Inc. and us (the "Caribou License"), we sublicense the rights of the Regents of the University of California and the University of Vienna (collectively, "UC/Vienna") to a worldwide patent portfolio that covers methods of use and compositions relating to engineered CRISPR/Cas9 systems for, among other things, cleaving or editing DNA and altering gene product expression in various organisms, including eukaryotic cells. We sublicense the UC/Vienna rights to this portfolio for human therapeutic, prophylactic and palliative uses, including companion diagnostics, except for anti-fungal and anti-microbial uses. This patent portfolio to-date includes, for example, multiple granted, allowed, and/or allowable patent applications in the U.S., as well as granted patents from the European Patent Office, the United Kingdom's Intellectual Property Office, the German Patent and Trade Mark Office, Australia's Intellectual Property agency and China's Intellectual Property Office, among others. Because UC/Vienna co-own this portfolio with Dr. Emmanuelle Charpentier (who has separately licensed her rights to other parties), we refer to this co-owned worldwide patent portfolio as the "UC/Vienna/Charpentier patent family."

Third parties could assert that our licensors, such as UC/Vienna/Charpentier, do not have rights to the licensed technology (such as the CRISPR/Cas9 technology in the case of the Caribou License), including inventorship and ownership rights to currently issued or allowable patents, or that any rights owned by our licensors, such as UC/Vienna/Charpentier, are limited. If such third parties were found to have rights to the licensed technology (such as CRISPR/Cas9 technology), we could be required to obtain rights from such parties or cease our development and commercialization efforts. For example, under our Caribou License, we have rights to patent applications owned by UC/Vienna/Charpentier covering certain aspects of CRISPR/Cas9 systems to edit genes in eukaryotic cells, including human cells (collectively, the "UC/Vienna/Charpentier eukaryotic patent family"). The Broad Institute, Massachusetts Institute of Technology, the President and Fellows of Harvard College and the Rockefeller University (collectively, the "Broad Institute") co-own patents and patent applications that also claim CRISPR/Cas9 systems to edit genes in eukaryotic cells (collectively, the "Broad Institute patent family"). Because the respective owners of various

UC/Vienna/Charpentier patent applications and the Broad Institute patent family both allege owning intellectual property claiming overlapping aspects of CRISPR/Cas9 systems and methods to edit genes in eukaryotic cells, including human cells, our ability to market and sell CRISPR/Cas9-based human therapeutics may be adversely impacted depending on the scope and actual ownership over the inventions claimed in the competing patent portfolios. On June 25, 2019, the Patent Trial and Appeal Board ("PTAB") of the U.S. Patent and Trademark Office ("USPTO") declared an interference between the UC/Vienna/Charpentier eukaryotic patent family and the Broad Institute patent family to determine which research group first invented the use of the CRISPR/Cas9 technology in eukaryotic cells and, therefore, is entitled to the U.S. patents covering that invention. The interference involved 14 allowable patent applications from the UC/Vienna/Charpentier eukaryotic patent family and 13 patents and one patent application from the Broad Institute patent family. On February 28, 2022, the PTAB issued a Decision of Priority and Judgment in the interference finding that the Broad Institute patent family has priority over the UC/Vienna/Charpentier patent family with respect to the subject matter of the interference. An appeal and cross-appeal from the interference are pending at the United States Court of Appeals for the Federal Circuit as Case Nos. 22-1594 and 22-1653, and the oral argument occurred on May 7, 2024.

On December 14, 2020, the PTAB declared an additional interference between the same 14 allowable patent applications in the UC/Vienna/Charpentier patent family, and one patent application owned by ToolGen, Inc. And, on June 21, 2021, the PTAB declared another interference between the same 14 allowable patent applications in the UC/Vienna/Charpentier patent family and one patent application owned by Sigma-Aldrich Co. LLC (a subsidiary of Merck KGaA). Because the patent applications involved in these interferences also purport to cover the use of CRISPR/Cas9 for gene editing in eukaryotic cells, the PTAB seeks to determine between the various groups which one invented first and is entitled to the resulting U.S. patents. A decision on motions issued in the ToolGen interference on September 28, 2022, and the priority phase of that interference was suspended until a mandate concludes the Federal Circuit appeal and cross-appeal in the UC/Vienna/Charpentier interference with the Broad Institute. The Sigma-Aldrich interference is in its motions phase, and an order scheduling oral argument issued on October 24, 2022. If either the Broad Institute, ToolGen or Sigma-Aldrich were to succeed in any of their respective interferences, the prevailing party or parties could seek to assert its issued patents against us based on our CRISPR/Cas9-based activities, including commercialization. In addition, the prevailing party may assert similar infringement claims against our existing or potential collaborators, clinical investigators, CMOs, CROs, consultants or vendors, and we may be obligated to defend and/or indemnify those parties against such infringement claims.

In addition, other third parties, such as Vilnius University and Harvard University, filed patent applications claiming CRISPR/Cas9-related inventions around or within a year after the first patent application filed in the UC/Vienna/Charpentier patent family and allege (or may allege) that they invented one or more of the inventions claimed by UC/Vienna/Charpentier before UC/Vienna/Charpentier. If the USPTO deems the scope of any of such third party's claims sufficiently overlap with the allowable claims from the applicable patent applications in the UC/Vienna/Charpentier patent family, the USPTO could declare other interference proceedings to determine the actual inventor of such claims. If these third parties were to prevail in their inventorship claims or obtain patent claims that cover our product candidates or related activities through these various legal proceedings, then we could be prevented from utilizing the intellectual property we have licensed from Caribou, as well as from developing and commercializing all or some of our products candidates unless we can obtain rights to the third parties' intellectual property or avoid or invalidate it.

Further, many third parties, including the third parties described above, have also filed patent applications and obtained patents covering aspects of the CRISPR/Cas9 technology in other key jurisdictions, including the EU members, the U.K., China and Japan. If these patents are deemed valid and cover our product candidates or related activities, we could be prevented from developing and commercializing all or some of our product candidates unless we license the relevant intellectual property or avoid it.

Defense of any potential infringement claims, regardless of their merit, would involve substantial litigation expense, would be a substantial diversion of management and other employee resources from our business and may impact our reputation. In the event of a successful claim of infringement against us, or a third party that we are obliged to defend and indemnify, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. In that event, we could be unable to further develop and commercialize our product candidates, which could harm our business significantly. Refer to "Item 1. Legal Proceedings" above for an example.

We depend on intellectual property licensed from third parties and termination or modification of any of these licenses could result in the loss of significant rights, which would harm our business.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others, including Caribou. Any termination of these licenses, loss by our licensors of the rights they receive from others, diminution of our rights or those of our licensors, or a finding that such intellectual property lacks legal effect, could result in the loss of significant rights and could harm our ability to commercialize any product candidates. For example, UC/Vienna could challenge Caribou's rights under their agreement, including Caribou's right to sublicense its rights to others, such as Intellia, and on what terms such a sublicense would be granted, each of which could adversely impact our rights under our agreement with Caribou. Similarly, Caribou or other licensors, or other third parties from which we derive rights, could challenge the scope of our licensed rights or fields under our license agreement, which could adversely impact our exclusive rights to use CRISPR/Cas9 technology in our human therapeutics field. For example, in connection with the arbitration regarding the scope of the Caribou License, we executed a leaseback agreement with Caribou granting it a sublicense to develop and commercialize CB-010, which is a chimeric antigen receptor T ("CAR-T") cell therapy directed at CD19. The leaseback agreement could adversely affect our business or that of our collaborators developing similar human therapeutics.

Disputes have and may arise between us and our licensors, our licensors and their licensors, or us and third parties that co-own intellectual property with our licensors or their licensors, regarding intellectual property subject to a license agreement, including those relating to:

- the scope of rights, if any, granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology, products and processes infringe on, or derive from, intellectual property of the licensor that is not subject to the license agreement;
- whether our licensor or its licensor had the right to grant the license agreement, or whether they are compliant with their contractual obligations to their respective licensor(s);
- whether third parties are entitled to compensation or equitable relief, such as an injunction, for our use of the intellectual property without their authorization;
- our right to sublicense patent and other rights to third parties, including those under collaborative development relationships;
- whether we are complying with our obligations with respect to the use of the licensed technology in relation to our development and commercialization of product candidates;
- our involvement in the prosecution, defense and enforcement of the licensed patents and our licensors' overall patent strategy;
- the allocation of ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and by us and our partners; and
- the amounts of royalties, milestones or other payments due under the license agreement.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, or are insufficient to provide us the necessary rights to use the intellectual property, we may be unable to successfully develop and commercialize the affected product candidates. If we or any such licensors fail to adequately protect this intellectual property, our ability to commercialize our products could suffer.

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

Patents relating to our product candidates are controlled by certain of our licensors or their respective licensors. Each of our licensors or their licensors generally has rights to file, prosecute, maintain and defend the patents we have licensed from such licensor. If these licensors or any future licensees and in some cases, co-owners from which we do not yet have licenses, having rights to file, prosecute, maintain, and defend our patent rights fail to adequately conduct these activities for patents or patent applications covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using or selling competing products. We cannot be certain that such activities by our licensors or their respective licensors have been or will be conducted in compliance with

applicable laws and regulations or in our best interests, or will result in valid and enforceable patents or other intellectual property rights. Pursuant to the terms of the license agreements with our licensors, the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and, even if we are permitted to pursue such enforcement or defense, we cannot ensure the cooperation of our licensors or, in some cases, other necessary parties, such as the co-owners of the intellectual property from which we have not yet obtained a license. We cannot be certain that our licensors or their licensors, and in some cases, their respective co-owners, will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. For example, with respect to our sublicensed rights from Caribou to UC/Vienna/Charpentier intellectual property, UC retained the right to control the prosecution, enforcement and defense of this intellectual property in its license agreement with Caribou and, pursuant to an Invention Management Agreement, shares these responsibilities with CRISPR Therapeutics AG and, under certain circumstances, ERS Genomics, Ltd., as the designated managers of the intellectual property. For these reasons, UC may be unable or unwilling to prosecute certain patent claims that would be best for our product candidates, or enforce its patent rights against infringers of the UC/Vienna/Charpentier patent family.

Even if we are not a party to legal actions or other disputes involving our licensed intellectual property, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. In addition, even when we have the right to control patent prosecution of licensed patents and patent applications, enforcement of licensed patents, or defense of claims asserting the invalidity of those patents, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to or after our assuming control.

We may not be successful in obtaining or maintaining necessary rights to product components and processes or other technology for our product development pipeline.

The growth of our business will likely depend in part on our ability to acquire or in-license additional proprietary rights. For example, our programs may involve additional product candidates, delivery systems or technologies that may require the use of additional proprietary rights held by third parties, including competitors. Our ultimate product candidates may also require specific modifications or formulations to work effectively and efficiently. These modifications or formulations may be covered by intellectual property rights held by others, including competitors. We may be unable to acquire or in-license any relevant third party intellectual property rights that we identify as necessary or important to our business operations.

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

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, may also be pursuing strategies to license or acquire third party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

If we are unable to successfully obtain rights to valid third party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

We may be required to pay certain milestones and royalties under our license agreements with third party licensors.

Under our current and future license agreements and other technology agreements, we may be required to pay milestones and royalties based on our revenues, including sales revenues of our products, utilizing the technologies acquired, licensed or sublicensed from third parties, including Caribou and Rewrite Therapeutics, Inc. ("Rewrite"), and these milestones and royalty payments could adversely affect our ability to research, develop and obtain approval of product candidates, as well as the overall profitability for us of any products that we may seek to commercialize. In order to maintain our intellectual property rights under these agreements, we will need to meet certain specified milestones, subject to certain cure provisions, in the development of our product candidates. Further, our counterparties, including our licensors (or their licensors) or licensees, may dispute the terms,

including amounts, that we are required to pay under the respective agreements. If these claims were to result in a material increase in the amounts that we are required to pay to our counterparties, including licensors or their licensors, or in a claim of breach of the applicable agreement, our ability to research, develop and obtain approval of product candidates, or to commercialize products, could be significantly impaired.

In addition, these agreements contain diligence milestones and we may not be successful in meeting all of the milestones in the future on a timely basis or at all. We will need to outsource and rely on third parties for many aspects of the clinical development, sales and marketing of our products covered under our license agreements and other technology agreements. Delay or failure by these third parties could adversely affect the continuation of these agreements with their counterparties, including our licensors or their licensors.

Risks Related to Patents and Trademarks

We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products or product candidates, or asserting and defending our intellectual property rights that protect our products and technologies.

We anticipate that we will file additional patent applications both in the U.S. and in other countries, as appropriate. However, we cannot predict:

- if and when any patents will issue;
- the scope, degree and range of protection any issued patents will afford us against competitors, including whether third parties will find ways to invalidate or otherwise circumvent our patents;
- whether others will apply for or obtain patents claiming aspects similar to those covered by our patents and patent applications;
- whether certain governments will appropriate our intellectual property rights and allow competitors to use them; or
- whether we will need to initiate litigation or administrative proceedings to assert or defend our patent rights, which may be costly whether we win or lose.

Composition of matter patents for biological and pharmaceutical products are generally considered to be the strongest form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of use. We cannot be certain, however, that any claims in our pending or future patent applications covering the composition of matter of our product candidates will be considered patentable by the USPTO or by patent offices in foreign countries, or that the claims in any of our ultimately issued patents will be considered valid and enforceable by courts in the U.S. or foreign countries. Method of use patents protect the use of a product for the specified method, for example a method of treating a certain indication using a product. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products “off-label” for those uses that are covered by our method of use patents. Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The strength of patents in the biotechnology and pharmaceutical field can be uncertain, and evaluating the scope of such patents involves complex legal and scientific analyses. The patent applications that we own or in-license may fail to result in issued patents with claims that cover any product candidates or uses thereof in the U.S. or in other foreign countries.

Further, the patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner, or in all jurisdictions. 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. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. We may also require the cooperation of our licensors or other necessary parties, such as the co-owners of the intellectual property from which we have not yet obtained a license, in order to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. and we may fail to seek or obtain patent protection in all major markets. For example, European patent law restricts the patentability of methods of treatment

of the human body more than U.S. law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we will be unable to know with certainty whether we were the first to make any inventions claimed in any patents or patent applications, or that we were the first to file for patent protection of such inventions, nor can we know whether those from whom we license patents were the first to make the inventions claimed or were the first to file.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the U.S. and abroad. There is a substantial amount of litigation as well as administrative proceedings for challenging patents, including interference, derivation, reexamination, and other post-grant proceedings before the USPTO and oppositions and other comparable proceedings in foreign jurisdictions, involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, and we expect this to be true for the CRISPR/Cas9 space as well. Indeed, a number of third parties have filed oppositions challenging the validity, and seeking the revocation, of several CRISPR/Cas9 genome editing patents granted to UC/Vienna/Charpentier by the European Patent Office ("EPO"). To date, UC/Vienna/Charpentier have successfully defended before the EPO's opposition division the validity of their first European patent, which covers compositions comprising Cas9 and single gRNA molecules, as well as methods of editing DNA *in vitro* or *ex vivo* using Cas9 and single gRNAs. The opponents to this patent have appealed the decision of the EPO's opposition division. If UC/Vienna/Charpentier fail in defending the validity of its first European patent, we may lose valuable intellectual property rights, such as the right to exclude others from using such intellectual property. Such an outcome could have a material adverse effect on our business in Europe. Similarly, third parties are opposing the other patents issued by the EPO to UC/Vienna/Charpentier, including their second European patent that was recently revoked by the EPO's opposition division, a decision that UC/Vienna/Charpentier have appealed. Although the claims of these other patents are more limited in scope compared to the first European patent, the inability to defend their respective validity could result in loss of valuable rights. In addition, since the passage of the America Invents Act in 2013, U.S. law also provides for other procedures to challenge patents, including *inter partes* reviews and post-grant reviews, that add uncertainty to the possibility of challenge to our developed or licensed patents and patent applications in the future. Furthermore, for U.S. applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. See the above risk factor entitled **"*Third party claims of intellectual property infringement against us, our licensors or our collaborators may prevent or delay our product discovery and development efforts*."**

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 practice the invention or 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 product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing their products to avoid being covered by our claims. If the breadth or strength of protection provided by the patent applications we hold is threatened, this could dissuade companies from collaborating with us to develop, and could threaten our ability to commercialize, product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market product candidates under patent protection would be reduced. Because patent applications in the U.S. and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates.

Our pending and future patent applications or the patent applications that we obtain rights to through in-licensing arrangements may not result in patents being issued which protect our technology or future product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Litigation or other administrative proceedings challenging our intellectual property, including interferences, derivation, reexamination, *inter partes* reviews and post-grant reviews, may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. Furthermore, there could be public announcement of the results of hearings, motions or other interim proceedings or developments in any proceeding challenging

the issuance, scope, validity and enforceability of our developed or licensed intellectual property. 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.

Any of these potential negative developments could impact the scope, validity, enforceability or commercial value of our patent rights and, as a result, have material adverse effect on our business, financial condition, results of operations or prospects.

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

We may in the future be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor or other claims challenging the inventorship of our patents or ownership of our intellectual property (including patents and intellectual property that we in-license). For example, the UC/Vienna/Charpentier patent family that is covered by our license agreement with Caribou is co-owned by UC/Vienna and Dr. Charpentier, and our sublicense rights are derived from the first two co-owners and not from Dr. Charpentier. Therefore, our rights to these patents are not exclusive and third parties, including competitors, may have access to intellectual property that is important to our business. In addition, we may have inventorship disputes arise from conflicting obligations of collaborators, consultants or others who are involved in developing our technology and product candidates. Litigation or other legal proceedings may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world.

We have limited intellectual property rights outside the U.S. Filing, prosecuting, maintaining and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. can have a different scope and strength than do those in the U.S. In addition, the laws of some foreign countries, such as China, Brazil, Russia, India and South Africa, do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as those in the U.S. These products may compete with our products and our patents or other intellectual property rights may not be effective or adequate to prevent them from competing. In addition, in jurisdictions outside the U.S., a license may not be enforceable unless all the owners of the intellectual property agree or consent to the license. Further, patients may choose to travel to countries in which we do not have intellectual property rights or which do not enforce these rights to obtain the products or treatment from competitors in such countries.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, such as China, Brazil, Russia, India and South Africa, do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to biopharmaceutical products, which could make it difficult in those jurisdictions for us to stop the infringement or misappropriation of our patents or other intellectual property rights, or the marketing of competing products in violation of our proprietary rights. Proceedings to enforce our patent and other intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, such proceedings could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims of infringement or misappropriation against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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

Competitors may infringe our patents or the patents of our licensors. To cease such infringement or unauthorized use, we may be required to file patent infringement claims, which can be expensive and time-consuming. In addition, in an infringement

proceeding or a declaratory judgment action against us, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

Interference or derivation proceedings provoked by third parties or brought by the USPTO may be necessary to determine the priority of inventions with respect to, or the correct inventorship of, our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Litigation, interference or derivation proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees.

Further, if a party to our licenses, either a licensee or licensor, were to breach or challenge our rights under the relevant license agreement (or if one of our licensor's own licensors were to challenge our licensor's rights), we may have to initiate or participate in a legal proceeding to enforce our rights. Any such legal proceeding could be expensive and time-consuming. In addition, if a court or other tribunal were to rule against us, we could lose key intellectual property and financial rights. Pursuing or defending against these legal claims, regardless of merits, would involve substantial legal expense and would be a substantial diversion of employee resources from our business. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or contractual litigation there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or proceeding. 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.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or before the USPTO or comparable foreign authority.

If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the U.S. or other jurisdictions, even outside the context of litigation. Such mechanisms include re-examination, *inter partes* review, post-grant review and equivalent proceedings in foreign jurisdictions, such as opposition or derivation proceedings. Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity, unpatentability and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. For example, as highlighted in the above risk factor entitled "***We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products or product candidates, or asserting and defending our intellectual property rights that protect our products and technologies***," various third parties have filed challenges to the validity of UC/Vienna/Charpentier's European patents, which cover compositions comprising Cas9 and gRNA molecules, as well as methods of editing DNA *in vitro* or *ex vivo* using Cas9 and gRNAs. If UC/Vienna/Charpentier fail in defending the validity of these patents, we may lose valuable intellectual property rights, such as the exclusive right to use such intellectual property. Such an outcome could have a material adverse effect on our business in Europe.

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

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. 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 patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. In any such event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

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

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or future, potential customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Risks Related to Potential Disclosure of Confidential Information

Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information.

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect our proprietary and confidential information. We also utilize proprietary processes for which it would be difficult to enforce patents. In addition, other elements of our product discovery and development processes involve proprietary know-how, information, or technology that is not covered by patents. Trade secrets, however, may be difficult to protect. We seek to protect our proprietary processes, in part, by entering into confidentiality agreements with our employees, consultants, outside scientific advisors, contractors, and collaborators, and we also rely on federal and state laws requiring our directors, employees, contractors and collaborators to protect our proprietary information. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, outside scientific advisors, contractors, and collaborators might intentionally or inadvertently disclose our trade secret information to competitors. In addition, competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the U.S. and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, or misappropriation of our intellectual property by third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results, and financial condition. Our trade secrets and other confidential information of ours may also be exposed through cybersecurity attacks, ransomware attacks, and other hacking attempts directed at our information technology systems and those of our employees, consultants, outside scientific advisors, contractors, vendors and collaborators. For more information, see the risk factor section entitled "Risks Related to Data and Privacy."

We may be subject to claims that our employees, directors, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies as well as academic research institutions. We may be subject to claims that we or our employees, directors, consultants, or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees' former employers. Litigation may be necessary to defend against these claims, which could result in money damages or a judicial order prohibiting the use of certain intellectual property. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

Risks Related to Our Financial Position and Need for Additional Capital

Risks Related to Past Financial Condition

We have never generated any revenue from product sales and our ability to generate revenue from product sales and become profitable depends significantly on our success in a number of areas.

We have no products approved for commercial sale, have not generated any revenue from product sales, and do not anticipate generating any revenue from product sales until we have received regulatory approval for the commercial sale of one of our product candidates. Our ability to generate revenue, and achieve and retain profitability, depends significantly on our success in many areas, including:

- obtaining regulatory approvals and marketing authorizations for our lead programs;
- obtaining market acceptance of our product candidates as viable treatment options;
- launching and commercializing product candidates for which we obtain regulatory approvals and marketing authorizations, either directly or with a collaborator or distributor;
- accurately assessing the size and addressability of potential patient populations;
- addressing any competing technological and market developments;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- avoiding infringement of or obtaining licenses to any valid intellectual property owned or controlled by third parties;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter or which may be necessary for us to develop, manufacture or commercialize our product candidates;
- maintaining good relationships with our collaborators and licensors;
- attracting, hiring and retaining qualified personnel;
- developing a sustainable and scalable manufacturing process for product candidates, including establishing and maintaining commercially viable supply relationships with third parties, such as CMOs, and potentially establishing our own manufacturing capabilities and infrastructure;
- successfully completing research, preclinical and clinical development of product candidates;
- investing resources in developing commercial manufacturing and operational infrastructure prior to clinical evidence of safety and efficacy for a given product candidate; and
- selecting commercially viable product candidates and effective delivery methods.

Even if one or more product candidates that we discover and develop are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate and the timing of such costs may be out of our control. If we are not able to generate revenue from the sale of any approved products, we may never become profitable.

Our operating history may make difficult the evaluation of our business's success to date and assessment of our future viability.

We are a clinical-stage company. We were founded and commenced operations in mid-2014. All of our product candidates are still in preclinical development or clinical trials. We have not yet demonstrated our ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture clinical and commercial scale therapeutics, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Our ability to generate product revenue or profits, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. We may never be able to develop or commercialize a marketable product.

Each of our programs may require additional discovery research and then preclinical and clinical development, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. In

addition, our product candidates must be approved for marketing by the FDA, or certain other foreign regulatory agencies, before we may commercialize any product.

Our operating history, particularly in light of the rapidly evolving genome editing field, may make it difficult to evaluate our current business and predict our future performance. Our relatively short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by clinical-stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

We have incurred net losses in each period since our inception, anticipate that we will continue to incur net losses in the future and may never achieve profitability.

We are not profitable and have incurred losses in each period since our inception. Our net loss was $390.1 million for the nine months ended September 30, 2024. As of September 30, 2024, we had an accumulated deficit of $2,048.5 million. We expect these losses to increase as we continue to incur significant research and development and other expenses related to our ongoing operations, seek regulatory approvals for our future product candidates, scale-up manufacturing capabilities, maintain, expand and protect our intellectual property portfolio and hire additional personnel to support the development of our product candidates and to enhance our operational, financial and information management systems. We expect to finance our operations through a combination of collaboration revenue, equity or debt financings or other sources, which may include collaborations with third parties.

A critical aspect of our strategy is to invest significantly in our technology to improve the efficacy and safety of potential product candidates that we discover. Even if we succeed in discovering, developing and ultimately commercializing one or more of these product candidates, we will continue to incur losses for the foreseeable future relating to our substantial research and development expenditures to develop our technologies. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. Further, the net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

Risks Related to Future Financial Condition

We may need to raise substantial additional funding to fund our operations. If we fail to obtain additional financing, we may be unable to complete the development and commercialization of any product candidates.

Our operations have required substantial amounts of cash since inception, and we expect to spend substantial amounts of our financial resources on our discovery programs going forward and future development efforts. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development, manufacture (or have manufactured) product candidates and components, and then conduct extensive clinical trials to demonstrate the safety and efficacy of any of our future product candidates in humans. Because preclinical and clinical testing is expensive and can take many years to complete, we may require additional funding to complete these undertakings. Further, if we are able to identify product candidates that are eventually approved, we will require significant additional amounts in order to launch and commercialize our product candidates. For the foreseeable future, we expect to continue to rely on additional financing to achieve our business objectives. Our future capital requirements will depend on and could increase significantly as a result of many factors, including the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our current or future product candidates, including additional expenses attributable to adjusting our development plans (including any supply related matters).

We will require additional capital for the further development and commercialization of any product candidates and may need to raise additional funds sooner if we choose to expand more rapidly than we presently anticipate or due to other unanticipated factors. Disruptions in the financial markets in general have made equity and debt financing more difficult to obtain, and may have a material adverse effect on our ability to meet our fundraising needs.

We cannot be certain that additional funding will be available on acceptable terms, or at all. We have no committed source of additional capital and if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development, manufacture or commercialization of our product candidates or other research and development initiatives. Our collaboration and license agreements may also be terminated if we are unable

to meet the payment or other obligations under the agreements. We could be required to seek collaborators for product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

Raising additional capital may cause dilution to our stockholders and restrict our operations.

We will need additional capital in the future to continue our planned operations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. In addition, the valuation of public companies may require selling equity at lower prices to ensure appropriate capitalization. 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 capital expenditures or declaring dividends.

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

Our results of operations could be adversely affected by general conditions in the national or global economy and financial markets. For example, governmental statements, actions or policies, political unrest and global financial crises can cause extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, political unrest or additional global financial crises, could result in a variety of risks to our business, including weakened demand for our products, if approved, or our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate, further political developments and financial market conditions could adversely impact our business.

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

The ability of the FDA and other similar regulatory agencies to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and authorization to accept the payment of user fees, reallocation of resources to address unique or new healthcare issues (or other future public health concerns), and statutory, regulatory, and policy changes. In addition, government funding of other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities.

If a prolonged government shutdown occurs in the U.S. or other jurisdictions where we plan to conduct our clinical trials, manufacturing, or other operations, it could significantly impact the ability of the relevant agency, such as the FDA, to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks Related to Manufacturing and Supply

In vivo *genome editing products and* ex vivo *engineered cell therapies based on CRISPR/Cas9 genome editing technology are novel and may be complex and difficult to manufacture. We could experience manufacturing problems that result in delays in the development, approval or commercialization of our product candidates or otherwise harm our business.*

The manufacturing process used to produce CRISPR/Cas9-based *in vivo* and engineered cell therapy product candidates may be complex, as they are novel and have not been validated for late phase clinical and commercial production and may require components that are difficult to obtain or manufacture at the necessary quantities and in accordance with regulatory requirements. Several factors could cause production interruptions, including equipment malfunctions; facility unavailability or contamination;

raw material cost, shortages or contamination; natural disasters, such as pandemics or other outbreaks or similar public health crises; disruption in utility services; human error; insufficient personnel; inability to meet legal or regulatory requirements; or disruptions in the operations of our suppliers.

Because our product candidates are regulated as biologics, their processing steps will be more complex than those of most small molecule drugs. Moreover, unlike small molecules, the physical and chemical properties of a complex product such as ours generally cannot be fully characterized. As a result, assays of the finished product or relevant components may not be sufficient to ensure that the product will perform in the intended manner. For this reason, we will employ multiple steps to control the manufacturing process to ensure that the process results in product candidates that meet their specifications, but complications at any one step could adversely impact our manufacturing of products. Further, we may encounter problems achieving adequate quantities and quality of clinical grade materials that meet the FDA or other relevant regulatory agency's applicable standards or our specifications with consistent and acceptable production yields and costs. Manufacturing process irregularities, even minor deviations from the normal process, could result in product defects or manufacturing issues that cause lot failures, product recalls, product liability claims and litigation, insufficient inventory or production interruption. In addition, product manufacturing and supply could be delayed if the FDA and other regulatory authorities require us to submit lot samples, testing results and protocols, or if they require that we not distribute a lot until they authorize the product's release.

Further, certain of our product candidates may require components that are unavailable or difficult to acquire or manufacture at the necessary scale and in compliance with regulatory requirements to support our clinical trials or, if approved, commercial efforts. We expect to continue to rely on third party CMOs to manufacture these components and the final product candidates for the foreseeable future. We may not have full control of these CMOs and they may prioritize other customers or be unable to provide us with enough manufacturing capacity to meet our objectives. Further, we may rely on CMOs outside the U.S. for certain components of our product candidates, and may be subject to importation regulations that may affect our ability to manufacture or increase the cost of our product candidates.

We also may encounter problems developing our own manufacturing capabilities, including hiring and retaining the experienced scientific, engineering, quality and manufacturing personnel needed to operate or supervise the necessary manufacturing processes. These issues could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements.

Any of these manufacturing and supply issues or delays could restrict our ability to meet clinical or market demand for our products, and be costly to us and otherwise harm our business, financial condition, results of operations and prospects. Further, any problems in manufacturing processes or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs.

Risks Related to Government Regulation

Risks Related to Obtaining Regulatory Approval

While the regulatory framework for approval of gene therapy including genome editing products exists, the limited precedent for genome-edited products makes the regulatory approval process potentially more unpredictable and we may experience significant delays in the clinical development and regulatory approval, if any, of our product candidates.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products, including genome editing therapeutics and engineered cell therapies, are subject to extensive regulation by the FDA in the U.S. and other regulatory authorities in other jurisdictions. For example, we are not permitted to market any drug or biological product, including *in vivo* products or engineered cell therapies, until we receive regulatory approval from the relevant regulatory agency, such as the FDA in the U.S. or EMA in the EU. We expect the novel nature of our product candidates to create challenges or raise questions from regulatory agencies in obtaining regulatory approval. For example, in the U.S., the FDA has not approved any *in vivo* gene editing-based therapeutic and has only approved one *ex vivo* CRISPR/Cas9 genome editing therapy for human therapeutic use. The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The Advisory Committee's opinion, although not binding, may significantly impact our ability to obtain approval of our product candidates. Moreover, while we are not aware of any specific genetic or biomarker tests for which regulatory approval would be necessary to advance any of our product candidates to clinical trials or commercialization, regulatory agencies could require the development and approval of such tests. Accordingly, the regulatory

approval pathway for such product candidates may be uncertain, complex, expensive and lengthy, as well as different in each jurisdiction, and approval may not be obtained in any, some or all jurisdictions.

Other non-regulatory entities may impact the regulatory agencies' and ethics committees' evaluation and approval decision regarding our product candidates. For example, in December 2018, the World Health Organization ("WHO") established the Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing. While the standards are expected to focus primarily on germline modifications, the guidelines could impact somatic cell editing research programs, such as ours. In March 2019, the WHO Expert Advisory Committee recommended initiating the first phase of a new global registry (the "Registry") to track research on human genome editing. Accepting this recommendation, the WHO announced plans in August 2019 for an initial phase of the registry using the International Clinical Trials Registry Platform. This phase will include worldwide registries for both somatic cell editing and germline editing clinical trials. Although registration of these clinical trials in the WHO's Registry currently is voluntary, failure to register could impact the evaluation by the regulators and ethics committees. In July 2021, the WHO Expert Advisory Committee issued recommendations and a governance framework for human genome editing research intended for the international, regional, national and institutional level. For example, the WHO recommended that clinical trials using somatic human genome editing technologies be reviewed and approved by the appropriate research ethics committee before inclusion in its Registry; basic and preclinical gene editing research also be included in a registry; somatic or germline human genome editing research should only take place in jurisdictions with domestic policy and oversight mechanisms; and relevant patent holders help ensure equitable access to human genome editing interventions. We cannot predict the impact of the WHO's current and future recommendations, or any policies or actions that ethics committees or regulatory agencies may take in response to such recommendations, on our research, clinical and business plans and results.

Patient enrollment is a significant factor in the timing of clinical trials and is affected by many factors, including willingness of physicians to use an experimental therapy, the availability of existing treatments, the trial's geographic locations and the number of patients in each geographic location. In addition, our ability to enroll and dose patients may be delayed by the relevant regulatory authority, as well as the IRB or another ethics committee (whether local or national). For example, as set forth in the National Institutes of Health ("NIH") Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules ("NIH Guidelines"), gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee ("IBC"), a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. Before a clinical trial can begin at any institution, that institution's IRB and its IBC assesses the safety of the research and identifies any potential risk to public health or the environment. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. Further, a clinical trial may be suspended or terminated by us, the relevant IRBs or ethics committees of the trial, or the FDA or other regulatory authorities, or upon a recommendation of the trial's DMC, due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience termination of, or delays in the completion of, any clinical trial of product candidates, the commercial prospects for such product candidates will be harmed, and our ability to generate product revenue will be impaired. In addition, any delays in completing any clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue.

We are currently conducting and may in the future conduct other clinical trials for our product candidates outside the U.S., and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We are currently conducting our Phase 3 clinical trial of NTLA-2001, and may in the future conduct clinical trials for our other product candidates outside the U.S. The acceptance of data from clinical trials conducted outside the U.S. or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. The FDA will generally not consider the data from a foreign clinical trial not conducted under an IND unless (i) the trial was well-designed and well-conducted in accordance with good clinical practice ("GCP") requirements, including requirements for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials in a way that provides assurance that the data and reported results are credible and accurate and that the rights, safety, and well-being of trial subjects are protected, and (ii) the FDA is able to validate the data from the trial through an onsite inspection, if necessary. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the

applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U.S. or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

We have received orphan drug designation for NTLA-2001 and NTLA-2002 and may in the future seek orphan drug designation for some of our other product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status, including market exclusivity, which may cause our revenue, if any, to be reduced.

Regulatory authorities in some jurisdictions, including the U.S. and Europe, may in response to a request from the sponsor designate products for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a 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 U.S., or a patient population of 200,000 or more in the U.S. when there is no reasonable expectation that the cost of developing and making available the product in the U.S. will be recovered from sales in the U.S. for that product. Orphan drug designation must be requested before submitting a BLA. In the U.S., orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the product and its potential orphan use are disclosed publicly by the FDA. In the EU, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the EU to justify the necessary investment in 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. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the approval of another marketing application for the same drug for the same indication for that time period. The applicable period is seven years in the U.S. and ten years in the EU (which can be extended to 12 years if the sponsor complies with an agreed-upon pediatric investigation plan). Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. In addition, the FDA can subsequently approve a marketing application for the same drug, or a product with the same active moiety, for treatment of the same disease or condition if it concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Similarly, the EMA may grant a marketing authorization to a similar medicinal product for the same indication as an authorized orphan product at any time if it is established that the second product, although similar, is safer, more effective or otherwise clinically superior to the authorized product. The FDA and EMA also can approve a different drug for the same orphan indication, or the same drug for a different indication, during the orphan exclusivity period.

We have received orphan drug designation from the FDA for NTLA-2001 for the treatment of ATTR amyloidosis and from the FDA and European Commission (“EC”) for NTLA-2002 for the treatment of HAE. We may seek orphan drug designation for some of our other product candidates in orphan indications in which there is a medically plausible basis for the use of these product candidates. Even where we obtain orphan drug designation, exclusive marketing rights in the U.S. may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. In addition, although we intend to seek orphan drug designation for other product candidates, we may never receive such designations.

The FDA may reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. In addition, proposed amendments to EU regulations regarding orphan medicines are under consideration that, if implemented, could reduce the current 10-year marketing exclusivity period in the EU for certain orphan medicines. Depending on what changes the FDA and the EC may make to their orphan drug regulations and policies, our business could be adversely impacted.

We have received regenerative medicine advanced therapy ("RMAT") designation by the FDA for NTLA-2002 for the treatment of HAE, and may in the future seek such designation for some of our other product candidates, but such designation may not actually lead to a faster development or regulatory review or approval process and we may be unable to obtain or maintain the benefits associated with such designation.

We have received the RMAT designation from the FDA for NTLA-2002 for the treatment of HAE. A product candidate is eligible for RMAT designation if: (1) it is a cell therapy, therapeutic tissue engineering product, human cell or tissue product, or a combination product using any such therapies or products; (2) it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) there is preliminary clinical evidence that indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. This program is intended to facilitate efficient development and expedite review of RMATs. A BLA for a product candidate with RMAT designation may be eligible for priority review or accelerated approval through (1) surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit or (2) reliance upon data obtained from a meaningful number of sites. Benefits of such designation also include early interactions with the FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A product candidate that has RMAT designation and is subsequently granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real-world evidence, such as electronic health records, the collection of larger confirmatory data sets, or post-approval monitoring of all patients treated with such therapy prior to its approval. RMAT designation is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for RMAT designation, the FDA may disagree and instead determine not to grant such designation. In any event, the receipt of RMAT designation for a product candidate may not result in a faster development process, review or approval compared to product candidates considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualifies for RMAT designation, the FDA may later decide that the product candidate no longer meets the conditions for qualification.

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

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA approves a product candidate, comparable regulatory authorities in foreign jurisdictions must also authorize the marketing and sale of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and review periods different from those in the U.S., including additional preclinical studies or clinical trials, as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the U.S., a product candidate must be approved for reimbursement before it can be sold in that jurisdiction. In some cases, the price that we are allowed to charge for our products is also subject to approval or to other legal restrictions.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the relevant regulatory requirements or to receive applicable marketing approvals, our target markets will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Risks Related to Ongoing Regulatory Obligations

Even if we receive regulatory approval of any product candidates or therapies, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.*

If any of our product candidates are approved, they may be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, distribution, storage, advertising, promotion, sampling, record-keeping, and submission of safety and efficacy data, and other post-market information and potential obligations (such as post-marketing studies), including both federal and state requirements in the U.S. and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with current good manufacturing practice ("cGMP") and GCP, and in certain cases, current good tissue practice ("cGTP") requirements for any clinical trials that we conduct post-approval.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, as applicable, including ensuring that quality control and manufacturing procedures conform to cGMP and, in certain cases, cGTP requirements, and applicable product tracking and tracing requirements. As such, we and our CMOs will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any BLA, other marketing applications, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. For example, the FDA or other regulatory agencies may also require a REMS or similar program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, we will have to comply with their respective legal or regulatory requirements including submissions of safety and other post-marketing information and reports and registration.

The FDA or other regulatory agencies may seek to impose consent decrees, withdraw approval or prohibit the export or import of a product if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

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

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the U.S. market, and the relevant foreign regulatory agencies do the same in their respective jurisdictions. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. In addition, the U.S. Supreme Court's June 2024 decision to overturn established case law giving deference to regulatory agencies' interpretations of ambiguous statutory language has introduced uncertainty regarding the extent to which the FDA's regulations, policies and decisions may become subject to increasing legal challenges, delays, and/or changes. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, we or our collaborators may lose any marketing approval that we or our collaborators may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Our employees, independent contractors, clinical investigators, CMOs, CROs, consultants, collaborators, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of non-compliance, fraud, misconduct or other illegal activity by our employees, independent contractors, clinical investigators, CMOs, CROs, consultants, collaborators, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to: comply with federal and state laws and those of other applicable jurisdictions; provide true, complete and accurate information to the FDA and other regulatory bodies in the U.S. or outside the U.S.; comply with manufacturing standards; comply with federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the U.S. and similar foreign privacy or fraudulent misconduct laws; or report financial information or data accurately; or disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the U.S., our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with clinical investigators and research patients, as well as proposed and future sales, marketing and education programs. In particular, the promotion, sales and marketing of healthcare products and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, including promotion and marketing of off-label uses of our products, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

The exit of the United Kingdom from the EU may result in an increased regulatory burden of conducting business in Europe.

The U.K.'s withdrawal from the EU ("Brexit"), became effective on January 31, 2020. On December 24, 2020, the U.K. and EU signed an EU-U.K. Trade and Cooperation Agreement ("TCA"), which became provisionally applicable on January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of cGMP, inspections of manufacturing facilities for medicinal products and cGMP documents issued, but does not provide for wholesale mutual recognition of U.K. and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework currently continues to apply in Northern Ireland). The regulatory regime in Great Britain therefore currently aligns for the most part with EU regulations; however, it is possible that these regimes will diverge more significantly in the future now that Great Britain's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of U.K. and EU pharmaceutical legislation.

For instance, the Clinical Trials Regulation which became effective in the EU on January 31, 2022 and provides for a streamlined clinical trial application and assessment procedure covering multiple EU Member States has not been implemented into U.K. law, and a separate application must be submitted for clinical trial authorization in the U.K. In addition, Great Britain is no longer covered by the centralized procedure for obtaining European Economic Area ("EEA")-wide marketing authorizations from the EMA for medicinal products and a separate process for authorization of drug products is required in Great Britain. On January 1, 2024, a new international recognition framework was put in place in the U.K. (known as the International Recognition Procedure ("IRP")), whereby the MHRA will have regard to decisions made by certain foreign regulators, including the EMA and the competent authorities of the EU Member States. Under this procedure, the MHRA will take into account the decision-making of such foreign regulators and will conduct a targeted assessment of the applications submitted through the IRP, but will retain the authority to reject applications if the evidence provided is considered insufficiently robust. Any delay in obtaining, or an inability to obtain, any regulatory approvals, as a result of Brexit or otherwise, would delay or prevent us from commercializing our current or future product candidates in the U.K. and could restrict our ability to generate revenue from that market.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.

We and many of our existing or potential collaborators, clinical investigators, CMOs, CROs, consultants or vendors are subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the U.S., numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), or by comparable laws in other jurisdictions. Depending on the facts and circumstances, we could be subject to civil, criminal, and administrative penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a covered entity in a manner that is not authorized or permitted by laws or regulations.

Compliance with U.S., both state and federal, and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our existing or potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

If we, or our collaborators, clinical investigators, CMOs, CROs, consultants or vendors, fail to comply with environmental, health and safety, and laboratory animal welfare laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We and many of our existing or potential collaborators, clinical investigators, CMOs, CROs, consultants or vendors are subject to numerous federal, state and local environmental, health and safety, and laboratory animal welfare laws and regulations. These legal requirements include those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes, as well as those which regulate the care and use of animals in research. Our operations, and those of our collaborators, clinical investigators, CMOs, CROs, consultants or vendors, acting on our behalf, may involve research using research animals and the use of hazardous and flammable materials, including chemicals and biological materials. Our operations, and those of our collaborators, clinical investigators, CMOs, CROs, consultants or vendors, acting on our behalf, also may produce hazardous waste products. We generally anticipate contracting with third parties for the disposal of these materials and waste. We will not be able to eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from any use by us of 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.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety, and laboratory animal welfare laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Failure to comply with labor and employment laws and regulations could subject us to legal liability and costs, including fines or penalties, as well as reputational damage that could harm our business.

We are subject to numerous federal, state and local laws and regulations relating to the recruiting, hiring, compensation and treatment of employees and contractors. These laws and regulations cover financial compensation (including wage and hour standards), benefits (including insurance and 401(k) plans), discrimination, workplace safety and health, and workers' compensation.

The Commonwealth of Massachusetts, where most of our employees are based, also has laws that expand on federal laws or create additional rights for employees or obligations for employers. For example, on July 1, 2018, the Massachusetts Equal Pay Act went into effect, which added protections employers must comply with regarding pay equity for "comparable work." In addition, on July 31, 2024, Massachusetts passed the Frances Perkins Workplace Equity Act, requiring disclosure of the pay range for a particular job under certain circumstances, including job postings, promotions, or when an employee requests. There is currently uncertainty regarding the exact scope of these new legal limits and such uncertainty may remain for the foreseeable future. We may face increased employment and legal costs to ensure we are complying with these laws.

On October 1, 2018, a new Massachusetts non-compete law went into effect, placing additional restrictions on employers seeking to enter into non-competition agreements with employees. Further, other jurisdictions in which our employees may work limit enforcement of non-competition agreements. For example, in California non-competition agreements with employees are generally unenforceable after termination of employment and Illinois contains strict laws affecting the enforcement of non-competition agreements. These non-compete laws may negatively impact our ability to prevent employees from working with direct or indirect competitors in the future and may affect our ability to retain key talent in a competitive market.

Our failure to comply with these and other related laws could expose us to civil and, in some cases, criminal liability, including fines and penalties. Further, government or employee claims that we have violated any of these laws, even if ultimately disproven, could result in increased expense and management distraction, as well as have an adverse reputational impact on us.

Risks Related to Our Reliance on Third Parties

Risks Related to Our Reliance on Collaboration Partners

Our technological advancements and any potential for revenue may be derived in part from our collaborations, including, for example, with Regeneron, and if the collaboration or co-development agreements related to a material collaboration were to be terminated or materially altered in an adverse manner, our business, financial condition, results of operations and prospects would be harmed.

We rely on strategic collaborations to advance our technology and co-develop products that we plan to co-commercialize. If our collaboration partner in a material collaboration fails to develop, obtain regulatory approval for or ultimately commercialize any product candidate from the development programs governed by the respective collaboration agreements, including, e.g., a co-development or co-commercialization agreement, or breaches or terminates our collaboration with it, our business, financial condition, results of operations and prospects could be harmed. In addition, any material alteration, in an adverse manner, of any material collaboration agreement, or dispute or litigation proceedings we may have related to a material collaboration in the future could delay development programs, create uncertainty as to ownership of or access to intellectual property rights, distract management from other business activities and generate substantial expense.

As described within Note 7, "Collaborations and Other Arrangements" of this Quarterly Report on Form 10-Q, we have entered into co-development and co-promotion arrangements with Regeneron. Regeneron may change its strategic focus or pursue alternative technologies in a manner that results in reduced, delayed or no revenue to us under these arrangements. For example, Regeneron has a variety of marketed products and product candidates either by itself or with other companies, including some of our competitors. In addition, the corporate objectives of our collaborators, such as Regeneron, may not be consistent with our best interests. Regeneron may change its position regarding its participation and funding of our joint activities, which may impact our ability to successfully pursue those programs.

Our existing and future collaborations will be important to our business. If we are unable to maintain any of these collaborations, or if these collaborations are not successful, our business could be adversely affected.

We have limited capabilities for product development and do not yet have any capability for sales, marketing or distribution. Accordingly, we have entered, and plan to enter, into collaborations with other companies, including our therapeutic-focused

collaboration agreements with Regeneron, which we believe can provide such capabilities. For example, in October 2023, we announced an expanded research collaboration with Regeneron to develop therapies for the treatment of neurological and muscular diseases. These current and future therapeutic-focused collaborations could provide us with important technologies and/or funding for our programs and technology. Our existing and future therapeutic collaborations may have a number of risks, including that collaborators:

- have significant discretion in determining the efforts and resources that they will apply;
- may not perform their obligations as expected;
- may dispute the amounts of payments owed;
- may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs or license arrangements based on clinical trial results, changes in their strategic focus or available funding, or external factors, such as a strategic transaction that may divert resources or create competing priorities;
- may delay, insufficiently fund, stop, initiate new or repeat clinical trials, reformulate a product candidate for clinical testing, or abandon a product candidate;
- could develop independently, or with third parties, products that compete directly or indirectly with our products and product candidates;
- may view product candidates discovered in our collaborations as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the development or commercialization of our product candidates;
- may dispute ownership or rights in jointly developed technologies or intellectual property;
- may fail to comply with applicable legal and regulatory requirements regarding the development, manufacture, sale, distribution or marketing of a product candidate or product;
- with sales, marketing, manufacturing and distribution rights to our product candidates may not commit sufficient resources to the product's sale, marketing, manufacturing and distribution;
- may disagree with us about material issues, including proprietary rights, contract interpretation, payment obligations or the preferred course of discovery, development, sales or marketing, which might cause delays or terminations of the research, development or commercialization of product candidates, lead to additional and burdensome responsibilities for us with respect to product candidates, or result in litigation or arbitration, any of which would be time-consuming and expensive;
- may not properly maintain or defend their or our relevant intellectual property rights or may use our proprietary information or sublicensed intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation and liability;
- may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- could become involved in a business combination or cessation that could cause them to deemphasize or terminate the development or commercialization of any product candidate licensed to it by us; and
- may terminate our collaborations, which could require us to raise additional capital to develop or commercialize the applicable product candidates, or lose access to the collaborator's intellectual property.

If our therapeutic collaborations do not result in the successful discovery, development and commercialization of products or if a collaborator terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. All of the risks relating to product discovery, development, regulatory approval and commercialization summarized and described in this report also apply to the activities of our therapeutic collaborators.

Additionally, if one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

As part of our business strategy, we may pursue acquisitions or licenses of assets or acquisitions of businesses, or disposition of assets or technologies. For example, in February 2022, we announced the acquisition of Rewrite in order to add additional capabilities to our growing platform, which acquisition included an exclusive license from the Regents of the University of California under certain patents related to DNA writing technology. We also may pursue strategic alliances and joint ventures that leverage our core technology and industry experience. If we decide to collaborate with other companies to discover, develop and commercialize therapeutic products, we face significant competition in seeking appropriate collaborators because, for example, third parties have comparable rights to the CRISPR/Cas9 system or similar genome editing technologies. In addition, we have limited experience with acquiring, disposing of or licensing assets or forming strategic alliances and joint ventures. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon 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. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail, delay or abandon discovery efforts or development programs, and the development, manufacture or commercialization of a product candidate, or increase our expenditures and undertake these activities at our own expense. If we elect to fund and undertake discovery, development, manufacturing or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary discovery, development, manufacturing and commercialization activities, we may not be able to further develop our product candidates, manufacture the product candidates, bring them to market or continue to develop our technology and our business may be materially and adversely affected. Furthermore, we may not identify or complete these transactions in a timely manner, on a cost-effective basis, or at all, and we may not realize the anticipated benefits of any acquisition, license, strategic alliance or joint venture.

Risks Related to Our Reliance on Other Third Parties

We currently rely, and expect to continue to rely in part on, third parties to manufacture our clinical product supplies, and we intend to rely on third parties for at least a portion of the manufacturing process of our product candidates, if approved. Our business could be harmed if the third parties fail to provide us with sufficient quantities of product inputs or fail to do so at acceptable quality levels or prices or fail to meet legal and regulatory requirements.

We are in the early stages of establishing our own manufacturing facility to provide preclinical, clinical and commercial supply of our product candidates and must rely on outside vendors, such as CMOs, to manufacture supplies and process our product candidates. We are manufacturing and processing product candidate components on a clinical scale and may not be able to successfully continue to do so. We are optimizing and will continue to optimize the manufacturing process for late-stage clinical and commercial supply, and cannot be sure that even minor changes in the process will result in therapies that are safe, pure and potent. We are also unable to predict how changing global economic conditions or ongoing geopolitical conflicts and related global economic sanctions, or potential global health concerns will affect our third party suppliers and manufacturers. Any negative impact of such matters on our third party suppliers and manufacturers may also have an adverse impact on our results of operations or financial condition.

Any facility that we may have in the future and the facilities used by our CMOs to manufacture our product candidates must be inspected and approved by, as applicable, the FDA or other foreign regulatory agencies after we apply for approval or marketing authorization. For the foreseeable future, we will be dependent on our CMO partners to properly manufacture adequate supply of our product candidates and components in a timely manner and in accordance with our specification. We also will depend on these entities for compliance with relevant legal and regulatory requirements for manufacture of our product candidates, including cGMP, and in certain cases, cGTP requirements. If we or our CMOs cannot successfully manufacture material that conforms to our specifications and the strict relevant regulatory requirements, we and our CMOs will not be able to secure or maintain regulatory approval for our respective manufacturing facilities. In addition, we have no control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel, particularly as we increase the scale of our manufactured material. If the FDA or relevant foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates.

If any CMO with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In such scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our product candidates may be unique to the original CMO and we may have difficulty transferring such skills to a back-up or alternate supplier, or we may be unable to

transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates or commercialize our products in a timely manner. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

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

We currently depend, and expect to continue to depend, upon third parties, including independent investigators, to conduct our clinical trials under agreements with universities, medical institutions, CROs, strategic partners and others. We expect to have to negotiate budgets and contracts with CROs, trial sites and other service and goods providers, which may result in delays to our development timelines and increased costs. For example, in February 2023, the U.S. Department of Justice investigated the research practices of a significant CRO with respect to their non-human primate imports. Issues of that nature may affect our ability to conduct preclinical studies that are required to advance our product candidates.

We currently rely, and expect to continue to rely heavily, on third parties over the course of our preclinical studies and clinical trials, and, as a result, will have limited control over the clinical investigators and other service providers, and limited visibility into their day-to-day activities, including with respect to their compliance with the approved clinical protocol and other legal, regulatory and scientific standards. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our legal responsibilities. We and these third parties are required to comply with GCP, which are regulations and guidelines enforced by the FDA, EMA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the relevant regulatory authorities may require us to suspend or terminate these trials or perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP requirements. In addition, our clinical trials must be conducted with product produced under cGMP, and in certain cases, cGTP, requirements and may require a large number of test articles for studies involving a large number of test patients.

Our or these third parties' failure to comply with these requirements or to recruit a sufficient number of patients may require us to delay, suspend, repeat or terminate clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates applicable federal, state or local, as well as foreign, laws and regulations, such as the fraud and abuse or false claims laws and regulations or privacy and security laws. In jurisdictions such as the U.K. and EU, penalties for violations of privacy laws and other regulations can be financially significant. Further, if any of our CROs, clinical investigators or others involved in our clinical trials fail to comply with such laws and regulations, we could be held responsible for its actions or omissions and be negatively impacted. In the event of non-compliance with the EU General Data Protection Regulation ("EU GDPR") and the EU GDPR in such form as incorporated into the laws of the U.K. ("U.K. GDPR," collectively with EU GDPR referred to as "GDPR"), we could be subject to substantial fines and other penalties, including fines of up to 20.0 million Euros (17.5 million GBP for the U.K. GDPR) or up to 4% of our total worldwide annual turnover for the preceding financial year, whichever is higher. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations.

Any third parties conducting our current or future clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third parties, we cannot control whether they devote sufficient time and resources to our ongoing preclinical, clinical, and nonclinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties fail to meet their contractual

obligations, legal requirements or expected deadlines, need to be replaced, or generate inaccurate or substandard clinical data by failing to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

A resurgence of the COVID-19 pandemic (or other future public health concern) and measures taken in response by U.S. or other governments may have a significant impact on our CROs, clinical sites and other service and goods providers, which may affect our ability to initiate and complete preclinical studies and clinical trials.

If any of our relationships with these third party CROs, clinical sites or other third parties terminate, we may not be able to enter into arrangements with alternative CROs, clinical sites or other third parties or to do so on commercially reasonable terms. Switching or adding additional CROs, clinical sites or other providers involves additional cost and requires management time and focus. In addition, the transition to a new CRO may result in delays, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with these parties, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

Risks Related to Data and Privacy

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

We are increasingly dependent upon information technology systems, infrastructure, and data to operate our business. In the ordinary course of business, we collect, store, and transmit large amounts of confidential information (including but not limited to intellectual property, such as trade secrets, 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 also outsourced elements of our operations to third parties, and as a result we manage a number of third party vendors who may or could have access to our confidential information. Our third party collaborators, vendors and service providers (including our CMOs and CROs) also have access to large amounts of confidential information relating to our operations, including our research and development efforts. The size and complexity of our information technology systems, and those of third party vendors, service providers and collaborators, and the large amounts of confidential information stored on those systems, make such systems potentially vulnerable to service interruptions or systems failures, or to cybersecurity incidents, breaches or compromises from inadvertent or intentional actions by our employees, third party vendors, service providers, collaborators, and/or business partners, or from cyber-attacks by malicious third parties.

In addition to such risks, the adoption of new technologies may also increase our exposure to cybersecurity incidents, breaches, compromises and failures. Further, having a significant portion of our workforce working from home for extended periods of time puts us at greater risk of cybersecurity attacks. Cyber-attacks are increasing in their frequency, sophistication, and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, denial-of-service attacks, attacks enhanced or facilitated by artificial intelligence (“AI”), social engineering, “phishing” scams, ransomware, network security breaches, and other means to affect service reliability and threaten the confidentiality, integrity, and availability of information. Certain of our service providers have been subject to such attacks in the past, and while no such attacks have resulted in a material impact to our business, our company or our service providers may be materially impacted by such attacks in the future. Significant disruptions to our information technology systems could adversely affect our business operations and/or result in the loss, misappropriation, and/or unauthorized access, use, or disclosure of, or the prevention of access to, confidential information (including but not limited to trade secrets or other intellectual property, proprietary business information, and personal information), and could result in financial, legal, business, and reputational harm to us and would adversely affect our operations, including our discovery and research and development programs. Any security incidents, compromises or breaches that lead to unauthorized access, use, or disclosure of personal information, including personal information regarding our employees or current or future clinical trial participants, could harm our reputation, require us to comply with onerous legal requirements under laws and regulations that protect the privacy and security of personal information, and subject us to significant liability including fines, litigation, and loss of current and future business.

Also, the loss of preclinical or clinical trial data from completed or future preclinical or clinical trials, respectively, could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure

of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed. Cybersecurity incidents, breaches, compromises, insider threats and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the types summarized and described above. While we have implemented security measures to protect our information technology systems and infrastructure, there is no assurance that such measures will prevent service interruptions or security breaches, incidents or compromises that could adversely affect our business.

Interruptions in the availability of server systems or communications with internet or cloud-based services, or failure to maintain the security, confidentiality, accessibility or integrity of data stored on such systems, could harm our business.

We rely upon a variety of internet service providers, third party web hosting facilities, cloud computing platform providers and software as a service ("SaaS") vendors to support our business. Failure to maintain the security, confidentiality, accessibility or integrity of data stored on such systems could result in interruptions in our operations, damage our reputation in the market, increase our service costs, cause us to incur substantial costs, subject us to liability for damages and/or fines, and divert our resources from other tasks, any one of which could materially adversely affect our business, financial condition, results of operations and prospects. If our security measures or those of our third party data center hosting facilities, cloud computing platform providers, SaaS vendors or third party service partners, are breached, and unauthorized access is obtained to our data or our information technology systems, we may incur significant legal and financial exposure and liabilities.

We also do not have control over the operations of the facilities of our cloud service providers, SaaS vendors or our third party web hosting providers, and they also may be vulnerable to damage or interruption from natural disasters, hardware or software outages, cybersecurity attacks, terrorist attacks and similar events or acts of misconduct. In addition, any changes in these providers' service levels may adversely affect our ability to meet our requirements and operate our business.

Social media platforms and artificial intelligence-based platforms present new risks and challenges to our business.

As social media continues to expand, it also presents us with new risks and challenges. Social media is increasingly being used to communicate information about us, our programs and the diseases our therapeutics are being developed to treat. Social media practices in the pharmaceutical and biotechnology industries are evolving, which creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media platforms to comment on the effectiveness of, or adverse experiences with, a product or a product candidate, which could result in reporting obligations or other consequences. Further, the accidental or intentional disclosure of non-public information by our workforce or others through media channels could lead to information loss. In addition, there is a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us, our products, or our product candidates on any social media platform. The nature of social media prevents us from having real-time control over postings about us on social media. We may not be able to reverse damage to our reputation from negative publicity or adverse information posted on social media platforms or similar mediums. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face restrictive regulatory actions or incur other harm to our business including quick and irreversible damage to our reputation, brand image and goodwill. While we have undertaken measures to restrict the use of public AI platforms, their use by people, including our vendors, suppliers and contractors, with access to our proprietary and confidential information, including trade secrets, may continue to increase and may lead to the release of such information, which may impact our ability to realize the benefit of our intellectual property.

Risks Related to Competition

We face significant competition in an environment of rapid technological change. The possibility that our competitors may achieve regulatory approval before we do or develop therapies that are more advanced or effective than ours may harm our business and financial condition or our ability to successfully market or commercialize our product candidates.

The biotechnology and pharmaceutical industries are extremely competitive in the race to develop new products. While we believe we have significant competitive advantages with our industry-leading expertise in genome editing, clinical development expertise and dominant IP position, we currently face and will continue to face competition for our development programs from companies that use genome editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities such as small molecules and antibodies. The competition is likely to come from multiple sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions. Many of these competitors may have access to greater capital and resources than us. For any products that we may ultimately commercialize, not only will we compete with any existing therapies and those therapies currently in development, but we will also have to compete with new therapies that may become available in the future.

Specific to our NTLA-2001 program, we are aware of other companies that are currently commercializing or developing products and therapies used to treat ATTR amyloidosis, including Alnylam Pharmaceuticals, Inc., AstraZeneca Pharmaceuticals LP, BridgeBio Pharma Inc., Ionis Pharmaceuticals, Inc., Metagenomi Technologies, LLC, Novo Nordisk A/S and Pfizer, Inc.

Specific to our NTLA-2002 program, we are aware of other companies that are currently commercializing or developing products used to treat HAE, including ADARx Therapeutics, Inc., Astria Therapeutics Inc., BioCryst Pharmaceuticals Inc., BioMarin Pharmaceuticals Inc., CSL Limited, Ionis Pharmaceuticals, Inc., KalVista Pharmaceuticals, Inc., Pharming Group N.V., Pharvaris N.V. and Takeda Pharmaceutical Company Limited.

Competitors in our efforts to provide other genetic therapies to patients can be grouped into at least three sets based on their product discovery platforms:

Our platform and product foci are on the development of therapies using CRISPR-based technologies. Genome editing companies focused on CRISPR-based technologies include: Beam Therapeutics Inc., Caribou Biosciences, Inc., CRISPR Therapeutics AG, Editas Medicine, Inc., Metagenomi Technologies, LLC, Prime Medicine, Inc., ToolGen, Inc. and Verve Therapeutics Inc.

There are also companies developing therapies using additional genome editing technologies, which include Allogene Therapeutics, Inc., bluebird bio, Inc., Cellectis S.A., Homology Medicines, Inc., Poseida Therapeutics, Inc., Precision Biosciences, Inc., Prime Medicine, Inc. and Sangamo Therapeutics, Inc.

We are also aware of companies developing therapies in various areas related to our specific research and development programs. For *ex vivo*, these companies include Allogene Therapeutics, Inc., Cellectis S.A., CRISPR Therapeutics AG and Precision BioSciences, Inc. For *in vivo*, these companies include CRISPR Therapeutics AG, Editas Medicine, Inc., Excision Biotherapeutics, Inc., Locus Biosciences, Inc., Metagenomi Technologies, LLC, Precision Biosciences, Inc. and Verve Therapeutics Inc.

Our competitors will also include companies that are or will be developing other genome editing methods as well as small molecules, biologics, *in vivo* gene therapies, engineered cell therapies and nucleic acid-based therapies for the same indications that we are targeting with our CRISPR/Cas9-based therapeutics.

Any advances in gene therapy, engineered cell therapies or genome editing technology made by a competitor may be used to develop therapies that could compete against any of our product candidates.

Many of these competitors have substantially greater research and development capabilities and financial, scientific, technical, intellectual property, manufacturing, marketing, distribution and other resources than we do, and we may not be able to successfully compete with them.

Even if we are successful in selecting and developing any product candidates, in order to compete successfully we may need to be first-to-market or demonstrate that our CRISPR/Cas9-based products are superior to therapies based on the same or different treatment methods. If we are not first-to-market or are unable to demonstrate such superiority, any products for which we are able to obtain approval may not be commercially successful. Furthermore, in certain jurisdictions, if a competitor has orphan drug status for a product and if our product candidate is determined to be contained within the scope of a competitor's orphan drug exclusivity, then approval of our product for that indication or disease could potentially be blocked, for example, for up to seven years in the U.S. and 10 years in the EU.

We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease our value and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations.

Risks Related to Commercialization

If, in the future, we are unable to establish sales, marketing and distribution capabilities or enter into agreements with third parties to sell, market and distribute products based on our technologies, we may not be successful in commercializing our products if and when any product candidates or therapies are approved and we may not be able to generate any revenue.

We do not currently have a sales, marketing or distribution infrastructure and, as a company, have no experience in the sale, marketing or distribution of therapeutic products. To achieve commercial success for any approved product candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services.
Factors that may inhibit our efforts to commercialize our product candidates include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future product candidates that we may develop;
- the lack of complementary treatments to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- the location of patients in need of our product candidates and the treating physicians who may prescribe the products; and
- unforeseen costs and expenses, as well as legal and regulatory requirements, associated with creating and operating a sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, we would likely have lower product revenue or profitability than if we ourselves were to market and sell our product candidates. In addition, we may be unable to enter into sales and marketing arrangements with third parties, or into arrangements with terms that are favorable to us. We likely will have little control over such third parties and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or through third parties, we may not be successful in commercializing our product candidates, and our business, results of operations, financial condition and prospects will be materially adversely affected.

Risks Related to Employee Matters and Managing Our Workforce

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

We are highly dependent on the research and development, clinical, manufacturing, commercialization, legal, financial and business development expertise of John M. Leonard, M.D., our President and Chief Executive Officer, James Basta, our Executive Vice President, General Counsel and Corporate Secretary, Eliana Clark, our Executive Vice President and Chief Technical Officer, Edward J. Dulac III, our Executive Vice President, Chief Financial Officer and Treasurer, Derek Hicks, our Executive Vice President and Chief Business Officer, David Lebwohl, our Executive Vice President and Chief Medical Officer, and Laura Sepp-Lorenzino, our Executive Vice President and Chief Scientific Officer, and Michael P. Dube, our Chief Accounting Officer, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment arrangements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees.

Execution of our business plans and strategies requires capable personnel with specialized skills and expertise in the research, development, manufacturing and commercialization of biopharmaceutical products, and, as a result, we may encounter difficulties in hiring or retaining capable personnel in key positions.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be important for our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives, and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products using our technology. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the

competition among numerous pharmaceutical and biotechnology companies, universities and research institutions for similar personnel. The market for qualified personnel in the biotechnology space generally, and genome editing and gene therapy fields in particular, in and around the Cambridge, Massachusetts area is especially competitive. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Further, some of the qualified personnel that we hire and recruit are not U.S. citizens, and there is uncertainty with regard to their future employment status due to the current U.S. administration's announced intention of modifying the legal framework for non-U.S. citizens to be employed in the U.S. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Risks Related to Healthcare

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, if approved, which could make it difficult for us to sell any product candidates or therapies profitably.

The success of our product candidates, if approved, depends on the availability of adequate coverage and reimbursement from third party payors, including government agencies, private health insurers and health maintenance organizations. There is significant uncertainty related to the insurance coverage and reimbursement of any newly approved product, but in particular novel genome editing and engineered cell products. All the therapeutic indications approved by the relevant authorities may not be covered or reimbursed. In addition, we cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates because they are novel treatments for diseases using a new technology and delivery approaches. For more information on coverage and reimbursement see the section entitled "**Business – Government Regulation and Product Approval – *Coverage and Reimbursement***" in our annual report on Form 10-K for the year ended December 31, 2023.

In the U.S. and some other jurisdictions, patients generally rely on third party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid in the U.S., and commercial payors are critical to new product acceptance.

Government authorities and other third party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. In the U.S., the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services ("CMS"), an agency within the U.S. Department of Health and Human Services. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare, and private payors often follow CMS's coverage decisions. Other jurisdictions have agencies, such as the National Institute for Health and Care Excellence in the U.K., that evaluate the use and cost-effectiveness of therapies, which impact the utilization and price of the medicine in such jurisdiction.

In the U.S., no uniform policy of coverage and reimbursement for products exists among third party payors. As a result, obtaining coverage and reimbursement approval of a product from a third party payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to each potential payor, with no assurance that coverage and adequate reimbursement will be obtained from all or any of them. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might be insufficient or may require co-payments that patients find unacceptably high, which may prevent us from achieving or sustaining profitability. Additionally, third party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of our genome editing products.

In addition, each country in which we seek approval to market our product candidates has unique laws and market practices regulating coverage and reimbursement for human therapeutics. Market acceptance and sales of our products in each country will depend on our ability to meet each of these jurisdiction's requirements for coverage and reimbursement. Further, changes to the country's existing requirements may also affect our ability to commercialize our products in the future, or achieve profitability from their sale.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, physician payment transparency laws, health information privacy and security laws and anti-corruption laws. If we are unable to comply, or have not fully complied, with such laws or their relevant foreign counterparts, we could face substantial penalties.

The sale, distribution and marketing of human therapeutics and our relationship with healthcare providers are strictly regulated by laws in the U.S. and most other jurisdictions in which we intend to seek approval for our product candidates. In addition, the collection and use of personal information, including Protected Health Information, is regulated by federal, state and foreign privacy, data security and data protection laws. Failure to comply with these laws could impair our ability to properly sell our product candidates in particular jurisdictions and subject us to liability from private and governmental entities. Addressing these diverse and sometimes contradictory requirements in myriad jurisdictions may necessitate that we expend significant resources on compliance efforts. Any failure to comply with these requirements may leave us exposed to possible enforcement actions and potential liability. For more information on these laws and regulations see the section entitled "**Business – Government Regulation and Product Approval – *Other Healthcare and Privacy Laws***" in our annual report on Form 10-K for the year ended December 31, 2023.

The scope and enforcement of each of these laws is not always certain and is subject to legislative, judicial or prosecutorial changes. Further, because of the breadth of these laws, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Indeed, U.S. federal and state enforcement bodies have increasingly scrutinized healthcare companies and providers interactions, which has led to a number of investigations, prosecutions, convictions and settlements in the industry. Ensuring business arrangements comply with applicable laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert the attention of our staff and resources from performing the duties required for the general operation of our business.

The increasingly global nature of our business operations, including clinical development efforts, subjects us to domestic and foreign anti-bribery and anti-corruption laws and regulations, such as the Foreign Corrupt Practices Act ("FCPA") and the U.K. Bribery Act. These activities create the risk of unauthorized payments or offers of payments that are prohibited under the FCPA, the U.K. Bribery Act or similar laws. It is our policy to implement safeguards to discourage these practices by our employees and agents. However, these safeguards may ultimately prove ineffective, and our employees, consultants, and agents may engage in conduct for which we might be held responsible. Violations of the FCPA may result in severe criminal or civil sanctions, and we may be subject to other liabilities, which could negatively affect our business, operating results and financial condition.

Further, the U.S. federal and state governments, as well as other jurisdictions, have myriad laws regulating the collection, storage, distribution, safeguarding and use of personal information of employees, patients, agents, and others. These different laws governing the privacy and security of health and other personal information often differ from each other in significant ways and may not have the same effective requirements, thus complicating efforts to comply with their respective provisions. For example:

- the California Consumer Privacy Act ("CCPA") requires covered companies to provide disclosures to California consumers and afford such consumers rights with respect to their personal information, including the rights to request deletion of their information, receive the information on record for them, know what categories of information are being maintained about them, and opt-out of certain sales of their information. The CCPA provides for civil penalties for violations, as well as a private right of action for certain data breaches that result in the loss of personal information, which may increase the likelihood of, and risks associated with, data breach litigation. The CCPA was amended by the California Privacy Rights Act ("CPRA"), which went into effect on January 1, 2023, and substantially modified the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information, establishing a state agency vested with the authority to enforce the CCPA and by creating additional obligations with respect to the processing of personal information, including regulating personal information collected about employees, applicants and retirees as well as that which is collected in a business to business capacity. We anticipate additional costs associated with CCPA and other U.S. state privacy law compliance and we cannot yet fully determine the impact that such laws, regulations and standards may have on our business;

- broad consumer privacy and data protection laws have been or are predicted to be passed in a number of additional states. Many state privacy and data protection laws differ from each other in significant ways, and it is not yet fully clear how these laws will be enforced and interpreted. In addition, other states have passed laws regulating specific aspects of privacy. For example, the State of Washington recently passed a law, effective as of March 31, 2024, that regulates health and medical information that is not subject to HIPAA. Similar laws have been passed in Connecticut and Nevada. Additionally, a small number of states have enacted laws that specifically target the collection and use of biometric information. Furthermore, other U.S. states have enacted stringent data security laws; and

•around the world, many countries have enacted laws that regulate data protection. In the EEA, the collection and use of personal data is regulated by the GDPR and the member states' related data protection and privacy laws. As the GDPR applies not only to businesses that are established within the EEA or the U.K. but also to any business that offers goods or services to individuals in those territories, it could apply to us. The GDPR imposes strict requirements, including requirements to ensure an appropriate legal basis or condition applies to the processing of personal data, special protections for "sensitive" personal data which includes health and genetic information of individuals in the EEA or the U.K.; expanded disclosures about the personal data use; information retention limitations; mandatory data breach notification requirements; and additional oversight obligations relating to third parties retained to process the personal data. The GDPR grants or enhances the rights of individuals with respect to their personal data, including the rights to object to the processing of the data and request deletion of the same. In addition, the GDPR includes strict requirements on, and prohibits, the transfer of personal data subject to GDPR to jurisdictions that have not been deemed by competent authorities to offer "adequate" privacy protections ("third countries"), unless a derogation exists or a valid GDPR transfer mechanism (for example, the EC approved Standard Contractual Clauses, certification to the EU-U.S. Data Privacy Framework (which allows for transfers for relevant U.S.-based organizations who self-certify compliance and participate in the framework) and the U.K. International Data Transfer Agreement/Addendum) has been put in place and a transfer impact assessment has been carried out. Our compliance with international data transfer obligations under the GDPR, where applicable, may require significant effort and cost, and may limit our ability to transfer such personal data to other jurisdictions or to work with certain service providers that process personal data, and may require us to make strategic considerations around where such personal data is stored. Further, although the EC has acknowledged that the U.K. currently has adequate protections for international data transfers, there may be post-Brexit developments in the future that result in additional costs and operational challenges in complying with the U.K. GDPR and any other developments regulating the transfer of personal data between the U.K. and EU. For example, the U.K. government has now introduced a Data Protection and Digital Information Bill (the "U.K. Bill") into the U.K. legislative process. The aim of the U.K. Bill is to reform the U.K.'s data protection regime following Brexit. If passed, the final version of the U.K. Bill may have the effect of further altering the similarities between the U.K. and EEA data protection regime and threaten the U.K. adequacy decision from the EC. Failure to comply with the requirements of the GDPR may result in warning letters, mandatory audits, orders to cease/change the use of data, and financial penalties, including fines of up to 4% of global revenues, or 20.0 million Euros (17.5 million GBP in the U.K.), whichever is greater. Moreover, data subjects can seek damages for violations, and non-profit organizations can bring claims on behalf of data subjects.

The costs associated with ensuring compliance with these laws, including in particular GDPR, may be onerous and may adversely affect our business, financial condition, results of operations and prospects. We may also need to rely on multiple third parties, such as partners and service providers, to meet these legal requirements, which could result in additional liability for us if they do not comply.

Efforts to ensure that we comply with all applicable healthcare and data privacy laws and regulations, as well as other domestic and foreign legal requirements, will involve substantial costs. It is possible that governmental and enforcement authorities in the U.S. or outside the U.S. will conclude that our business practices do not comply with current or future legal requirements. If any noncompliance actions are instituted against us, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, individual imprisonment, exclusion from participation in federal healthcare programs (such as Medicare and Medicaid), contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, any of which could adversely affect our ability to operate our business and affect the results of our operations. Any action alleging a violation of these laws, even if successfully defended, could result in significant legal expenses and divert management's attention from the operation of the business. Prohibitions or restrictions on sales (including importation or exportation) or withdrawal of future marketed products could materially affect business in an adverse way.

Healthcare cost control initiatives, including healthcare legislative and regulatory reform measures, may have a material adverse effect on our business and results of operations.

The U.S. and many other jurisdictions have enacted or proposed legal changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates, affect our ability to profitably sell our product candidates once approved, and restrict or regulate post-approval activities. Changes in the legal requirements, or their interpretation, could impact our

business by compelling, for example, modification to: our manufacturing arrangements; product labeling; pricing and reimbursement arrangements; private or governmental insurance coverage; the sale practices for, or availability of, our products; or record-keeping activities. If any such changes were to be imposed, they could adversely affect the operation of our business. For more information on these laws and regulations see the section entitled "**Business – Government Regulation and Product Approval – *Healthcare Reform***" in our annual report on Form 10-K for the year ended December 31, 2023.

Third party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In the U.S. and certain other jurisdictions, there have been, and are expected to continue to be, a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. In the U.S., however, significant uncertainty exists regarding the provision and financing of healthcare because the newly elected administration and federal legislators have publicly declared their intention to review and potentially significantly modify the current legal and regulatory framework for the healthcare system.

We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our approved products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

Risks Related to Our Common Stock

Risks Related to Investment in Securities

An active trading market for our common stock may not be sustained.

If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or sell their shares at or above the prices at which they acquired their shares or sell their shares at the time they would like to sell. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

The price of our common stock historically has been volatile, which may affect the price at which you could sell any shares of our common stock.

The market price for our common stock historically has been highly volatile and could continue to be subject to wide fluctuations in response to various factors. This volatility may affect the price at which you could sell the shares of our common stock, and the sale of substantial amounts of our common stock could adversely affect the price of our common stock. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and other factors, including:

- the success of our products or technologies or competing products or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- developments or disputes concerning issued patents, patent applications or other intellectual property rights;
- regulatory or legal developments in the U.S. and other countries;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;

- the results of our efforts to discover, develop, manufacture, acquire or in-license our current and additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or the financial results of companies that are perceived to be similar to us;
- sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- public perception of the safety of genome editing based therapeutics;
- general economic, industry and market conditions; and
- the other factors summarized and described in this *Risk Factors* section.

Companies trading in the stock market in general, and in The Nasdaq Global Market in particular, have also experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

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

The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts may not publish an adequate amount of research on us, which may negatively impact the trading price for our stock. In addition, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. Further, if our operating results fail to meet the forecasts of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

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

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

Risk Related to Ownership Generally

Our principal stockholders and management own a significant percentage of our stock and, if they choose to act together, will be able to control or exercise significant influence over matters subject to stockholder approval.*

Our executive officers, directors, 5% or greater stockholders and their affiliates beneficially own a significant percentage of our outstanding voting stock. These stockholders may have the ability to influence us through their ownership positions. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We have broad discretion over the use of our cash, cash equivalents and marketable securities, and may not use them effectively, including that we may be exposed to liquidity issues and other systemic financial risks at the financial institutions holding our cash and cash equivalents.

Our management has broad discretion to use our cash, cash equivalents and marketable securities to fund our operations and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending our use to fund operations, we may invest our cash, cash equivalents and marketable securities in a manner that does not produce income or that loses value.

A portion of our cash may be held by financial institutions that may have been, or could in the future become, exposed to liquidity issues, bank failures or other systemic financial risks. Our uninsured cash deposits with such financial institutions may be at risk in the event they experience liquidity problems or other financial losses. For example, in May 2023, the Federal Deposit Insurance Corporation ("FDIC") took control of First Republic Bank and JP Morgan Chase & Co. has since acquired a substantial amount of assets and certain liabilities of First Republic. Although the U.S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to $25.0 billion of loans to financial institutions secured by certain government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, there is no guarantee that such loans will fully mitigate the risk of potential losses or that the U.S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion. We assess our banking relationships as we believe necessary or appropriate, but uncertainty remains over liquidity concerns in the broader financial services industry, and our business, our business partners, or industry as a whole may be adversely impacted in ways that we cannot predict at this time, including our ability to access cash in amounts adequate to finance or capitalize our current and/or projected business operations could be significantly impaired by factors that affect the financial institutions with which we have banking relationships, and in turn, us. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements (including cash management arrangements), disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. In addition, our vendors, such as our CMOs, CROs or business partners, may be susceptible to the foregoing liquidity or other financial risks and factors, which could, in turn, have a material adverse effect on our current and/or projected business operations and results of operations and financial condition.

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

As a public company, and particularly since we are no longer an "emerging growth company" under applicable SEC regulations, we incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Market 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. Our management and other personnel devote a substantial amount of time to these compliance initiatives.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 ("Section 404"), we are required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. We conduct a process each year to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we dedicate internal resources, engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements.

Risks Related to Future Financial Condition

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

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. 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. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Given the volatility in the capital markets, we may not be willing or able to continue to raise equity capital. We may, therefore, need to turn to other sources of funding that may have terms that are not favorable to us, or reduce our business operations given capital constraints. In addition, sales of a substantial number of shares of our outstanding common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. We cannot predict the effect that future sales of common stock or other equity-related securities would have on the market price of our common stock. Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

Risks Related to our Charter and Bylaws

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us difficult, limit attempts by our stockholders to replace or remove our current management and adversely affect our stock price.

Provisions of our certificate of incorporation and by-laws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our stock. Among other things, the certificate of incorporation and by-laws:

- permit the board of directors to issue up to 5,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that the authorized number of directors may be changed only by resolution of the board of directors;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide the board of directors into three classes;
- provide that a director may only be removed from the board of directors by the stockholders for cause;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders, and may not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner, and meet specific requirements as to the form and content of a stockholder's notice;
- prevent cumulative voting rights (therefore allowing the holders of a plurality of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- require that, to the fullest extent permitted by law, a stockholder reimburse us for all fees, costs and expenses incurred by us in connection with a proceeding initiated by such stockholder in which such stockholder does not obtain a judgment on the merits that substantially achieves the full remedy sought;
- provide that special meetings of our stockholders may be called only by the chairman of the board, our chief executive officer (or president, in the absence of a chief executive officer) or by the board of directors; and

•provide that stockholders will be permitted to amend the bylaws only upon receiving at least two-thirds of the total votes entitled to be cast by holders of all outstanding shares then entitled to vote generally in the election of directors, voting together as a single class.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any "interested" stockholder for a period of three years following the date on which the stockholder became an "interested" stockholder.

Our certificate of incorporation and by-laws designate certain courts as the sole and exclusive forums for certain disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our certificate of incorporation and by-laws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for any state law claims for any derivative action or proceeding brought on our behalf alleging state law claims, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our by-laws, any action to interpret, apply, enforce, or determine the validity of our certificate of incorporation or bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine (the "Delaware Forum Provision"). The Delaware Forum Provision does not apply to claims arising under the Exchange Act or the Securities Act. Our by-laws further provide that the U.S. District Court for the District of Massachusetts will be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the "Federal Forum Provision"). We have chosen the U.S. District Court for the District of Massachusetts as the exclusive forum for such Securities Act causes of action because our principal executive offices are located in Cambridge, Massachusetts. Our by-laws provide that any person or entity purchasing or otherwise acquiring any interest in any shares of our common stock is deemed to have notice of and consented to the foregoing Delaware Forum Provision and the Federal Forum Provision.

The Delaware Forum Provision and the Federal Forum Provision may impose additional litigation costs on stockholders in pursuing the claims identified above, particularly if the stockholders do not reside in or near the State of Delaware or the Commonwealth of Massachusetts. Additionally, the Delaware Forum Provision and the Federal Forum Provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find the Delaware Forum Provision and the Federal Forum Provision to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition. The Court of Chancery of the State of Delaware or the U.S. District Court for the District of Massachusetts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

Risks Related to Tax Matters

Changes in tax law may adversely affect our business and financial condition.

The laws and rules dealing with U.S. federal, state and local income taxation are routinely being reviewed and modified by governmental bodies, officials and regulatory agencies, including the Internal Revenue Service and the U.S. Treasury Department. Since we were founded in 2014, many such changes have been made and changes are likely to continue to occur in the future. We cannot predict whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or issued, that could result in an increase in our or our stockholders' tax liability.

Our ability to use our net operating loss ("NOL") carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. As of December 31, 2023, we had federal and state NOLs of $954.0 million and $922.8 million, respectively, some of which begin to expire in 2034. Federal and certain state NOLs generated in taxable years ending after December 31, 2017 are not subject to expiration. As of December 31, 2023, we had federal and state research and development and other credit carryforwards of approximately $100.7 million and $64.1 million, which begin to expire in 2034 and 2029, respectively. Under Sections 382 and 383 of the Code, if a corporation undergoes an "ownership

change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, the corporation's ability to use its pre-change NOLs, and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. During 2022, we completed an assessment of the available net operating loss carryforwards and other tax attributes under Section 382 that covered the period from inception through December 31, 2022. This analysis did not result in a material limitation to our other tax attributes. We have not completed an analysis through December 31, 2023. To the extent there was a change in control during 2023, our tax attributes could be subject to limitation. We may experience ownership changes in the future. As a result, if we earn net taxable income, our ability to use our pre-change NOLs and research and development tax credits to offset such taxable income and income tax, respectively, could be subject to limitations. Similar provisions of state tax law may also apply. As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

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

None.

Item 5. Other Information

Rule 10b5-1 Trading Plans

The following table describes for the three months ended September 30, 2024 each trading arrangement under which the Company's directors or officers adopted, materially modified, or terminated any contract, instruction, or written plan for the purchase or sale of Company securities that was intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) or any non-Rule 10b5-1 trading arrangement.

Name *(Title)*	Action Taken *(Date of Action)*	Type of Trading Arrangement	Nature of Trading Arrangement	Duration of Trading Arrangement	Aggregate Number of Securities
James E. Basta *(EVP, General Counsel)*	Adoption *(July 11, 2024)*	Rule 10b5-1 trading arrangement	Sale	Until the earlier of (a) November 11, 2024; (b) the first date on which all trades have been executed or all trading orders related to such trades have expired; and (c) the date on which the plan holder gives notice to terminate the plan.	Indeterminable (1)
Muna Bhanji *(Director)*	Adoption *(September 27, 2024)*	Rule 10b5-1 trading arrangement	Sale	Until the earlier of (a) June 20, 2025; (b) the first date on which all trades have been executed or all trading orders related to such trades have expired; and (c) the date on which the plan holder gives notice to terminate the plan.	3,624

(1) The number of shares that will be sold in accordance with this trading arrangement is indeterminable at the time of the filing of this Quarterly Report on Form 10-Q for the period ended September 30, 2024. Upon vesting of RSUs, it is the Company's policy to immediately initiate a sell-to-cover in order to satisfy any applicable tax withholding obligations on behalf of the employee. The number of shares sold in the sell-to-cover will vary based on the market price of the Company's common stock at the time of settlement. Any remaining shares held by Mr. Basta after the sell-to-cover may be sold pursuant to the terms of this trading arrangement.

Item 6. Exhibits

The following exhibits are incorporated by reference or filed as part of this report.

3.1	Second Amended and Restated Certificate of Incorporation of the Registrant. (incorporated by reference to the Registrant's Annual Report on Form 10-K (File No. 001-37766) filed with the Securities and Exchange Commission on February 22, 2024).
3.2	Second Amendment to the Second Amended and Restated Certificate of Incorporation of the Registrant dated June 12, 2024 (incorporated by reference to the Registrant's Current Report on Form 8-K (File No. 001-37766) filed with the Securities and Exchange Commission on June 13, 2024).
3.3	Second Amended and Restated By-laws of the Registrant. (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37766), filed with the Securities and Exchange Commission on May 7, 2020).
31.1	Certification of the Chief Executive Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. (1)
31.2	Certification of the Chief Financial Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. (1)
32.1	Certifications pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of The Sarbanes-Oxley Act of 2002, by John M. Leonard, M.D., President and Chief Executive Officer of the Company, and Edward J. Dulac III, Executive Vice President, Chief Financial Officer of the Company. (2)
101.INS	Inline XBRL Instance Document (1)
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents. (1)
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101) (1)

(1)Filed with this Quarterly Report on Form 10-Q.
(2)The certifications furnished in Exhibit 32.1 hereto are deemed to accompany this Quarterly Report on Form 10-Q and will not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended. Such certifications will not be deemed to be incorporated by reference into any filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

SIGNATURES

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

Dated: November 7, 2024

INTELLIA THERAPEUTICS, INC.

By: /s/ John M. Leonard
John M. Leonard, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

By: /s/ Edward J. Dulac III
Edward J. Dulac III
Executive Vice President, Chief Financial Officer
(Principal Financial Officer)

By: /s/ Michael P. Dube
Michael P. Dube
Vice President, Chief Accounting Officer
(Principal Accounting Officer)

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER PURSUANT TO RULE 13a-14(a) / RULE 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

I, John M. Leonard, M.D., certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: November 7, 2024

/s/ John M. Leonard
John M. Leonard, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER PURSUANT TO
RULE 13a-14(a) / RULE 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

I, Edward J. Dulac III, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: November 7, 2024

/s/ Edward J. Dulac III
Edward J. Dulac III
Executive Vice President, Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

**CERTIFICATIONS OF CEO AND CFO PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with this Quarterly Report on Form 10-Q of Intellia Therapeutics, Inc. (the "Company") for the period ended September 30, 2024, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned, John M. Leonard, M.D., President and Chief Executive Officer (Principal Executive Officer) of the Company, and Edward J. Dulac III, Executive Vice President and Chief Financial Officer (Principal Financial Officer) of the Company, hereby certifies, pursuant to 18 U.S.C. (section) 1350, as adopted pursuant to (section) 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

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

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

Dated: November 7, 2024

/s/ John M. Leonard
John M. Leonard, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

/s/ Edward J. Dulac III
Edward J. Dulac III
Executive Vice President and Chief Financial Officer
(Principal Financial Officer)