

**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, 2023

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
(State or Other Jurisdiction of
Incorporation or Organization)

40 Erie Street, Suite 130, Cambridge, Massachusetts
(Address of Principal Executive Offices)

36-4785571
(I.R.S. Employer
Identification No.)

02139
(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	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
Emerging growth company	<input type="checkbox"/>		

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 3, 2023: 89,554,891 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, 2023	December 31, 2022
ASSETS		
Current Assets:		
Cash and cash equivalents	\$ 168,027	\$ 523,506
Marketable securities	686,761	669,116
Accounts receivable (\$0 and \$0.3 million, respectively, from related party)	6,491	3,768
Prepaid expenses and other current assets	32,214	20,407
Total current assets	893,493	1,216,797
Marketable securities - noncurrent	137,752	69,338
Property and equipment, net	33,800	27,921
Operating lease right-of-use assets	118,775	133,076
Equity method investment	17,166	32,455
Investments and other assets	42,363	40,527
Total Assets	<u>\$ 1,243,349</u>	<u>\$ 1,520,114</u>
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	\$ 3,553	\$ 5,154
Accrued expenses (\$1.0 million and \$1.6 million, respectively, from related party)	57,979	60,876
Current portion of operating lease liability	17,074	16,685
Current portion of deferred revenue (\$0 and \$19.9 million, respectively, from related party)	13,347	43,839
Total current liabilities	91,953	126,554
Deferred revenue, net of current portion	12,719	19,932
Long-term operating lease liability	101,263	114,018
Contingent consideration liability	-	24,026
Total liabilities	205,935	284,530
Commitments and contingencies (Note 6)		
Stockholders' Equity:		
Common stock, \$0.0001 par value; 240,000,000 and 120,000,000 shares authorized at September 30, 2023 and December 31, 2022, respectively; 89,097,821 and 87,103,007 shares issued and outstanding at September 30, 2023 and December 31, 2022, respectively	9	9
Additional paid-in capital	2,567,195	2,420,223
Accumulated other comprehensive loss	(3,572)	(7,461)
Accumulated deficit	(1,526,218)	(1,177,187)
Total stockholders' equity	1,037,414	1,235,584
Total Liabilities and Stockholders' Equity	<u>\$ 1,243,349</u>	<u>\$ 1,520,114</u>

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)

	<u>Three Months Ended September 30,</u>		<u>Nine Months Ended September 30,</u>	
	2023	2022	2023	2022
Collaboration revenue (1)	\$ 11,992	\$ 13,266	\$ 38,192	\$ 38,548
Operating expenses:				
Research and development	113,696	96,651	326,088	319,945
General and administrative	29,403	22,145	87,503	66,680
Total operating expenses	<u>143,099</u>	<u>118,796</u>	<u>413,591</u>	<u>386,625</u>
Operating loss	(131,107)	(105,530)	(375,399)	(348,077)
Other income (expense), net:				
Interest income	12,740	1,945	37,373	3,188
Loss from equity method investment	(3,857)	(1,834)	(10,905)	(7,831)
Change in fair value of contingent consideration	-	(7,810)	(100)	(8,059)
Total other income (expense), net	<u>8,883</u>	<u>(7,699)</u>	<u>26,368</u>	<u>(12,702)</u>
Net loss	<u>\$ (122,224)</u>	<u>\$ (113,229)</u>	<u>\$ (349,031)</u>	<u>\$ (360,779)</u>
Net loss per share, basic and diluted	<u>\$ (1.38)</u>	<u>\$ (1.49)</u>	<u>\$ (3.96)</u>	<u>\$ (4.78)</u>
Weighted average shares outstanding, basic and diluted	<u>88,645</u>	<u>76,047</u>	<u>88,204</u>	<u>75,543</u>
Other comprehensive loss:				
Unrealized gain (loss) on marketable securities	142	991	1,649	(5,069)
Other comprehensive gain (loss) from equity method investment	154	(805)	2,240	(1,667)
Comprehensive loss	<u>\$ (121,928)</u>	<u>\$ (113,043)</u>	<u>\$ (345,142)</u>	<u>\$ (367,515)</u>
(1) Including the following revenue from related party (see Notes 7 and 8):	\$ 1,946	\$ 4,414	\$ 12,673	\$ 15,612

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,	
	2023	2022
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	\$ (349,031)	\$ (360,779)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	6,510	5,541
Loss (gain) on disposal of property and equipment	5	(162)
Equity-based compensation	99,007	66,774
(Accretion) amortization of investment discounts and premiums	(19,590)	5,252
Loss from equity method investment	10,905	7,831
Deferral of equity method investment intra-entity profit on sales	6,624	8,530
Change in fair value of contingent consideration	100	8,059
In-process research and development expense	-	55,990
Changes in operating assets and liabilities:		
Accounts receivable	(2,723)	(1,992)
Prepaid expenses and other current assets	(11,806)	(228)
Operating lease right-of-use assets	14,148	8,516
Other assets	(836)	(982)
Accounts payable	(1,419)	(5,334)
Accrued expenses	(3,008)	12,852
Deferred revenue	(37,705)	(46,739)
Operating lease liabilities	(12,213)	(6,547)
Net cash used in operating activities	(301,032)	(243,418)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	(12,465)	(9,646)
Purchases of marketable securities	(754,689)	(192,598)
Maturities of marketable securities	689,868	437,387
Proceeds from sale of property and equipment	-	150
Acquired in-process research and development, net of cash acquired of \$287	-	(44,832)
Net cash (used in) provided by investing activities	(77,286)	190,461
CASH FLOWS FROM FINANCING ACTIVITIES:		
Net proceeds from issuance of common stock through at-the-market offerings	16,184	62,140
Proceeds from options exercised	5,604	13,984
Issuance of shares through employee stock purchase plan	2,051	1,068
Net cash provided by financing activities	23,839	77,192
Net (decrease) increase in cash, cash equivalents and restricted cash equivalents	(354,479)	24,235
Cash, cash equivalents and restricted cash equivalents, beginning of period	535,463	125,486
Cash, cash equivalents and restricted cash equivalents, end of period	\$ 180,984	\$ 149,721
Reconciliation of cash, cash equivalents and restricted cash equivalents to condensed consolidated balance sheet:		
Cash and cash equivalents	\$ 168,027	\$ 141,194
Restricted cash equivalents, included in investments and other assets	12,957	8,527
Total cash, cash equivalents and restricted cash equivalents	\$ 180,984	\$ 149,721
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Purchases of property and equipment unpaid at period end	\$ 1,552	\$ 2,180
Shares issued for Rewrite contingent consideration	24,126	-
Right-of-use asset acquired under operating lease	-	30,663
Contingent consideration liability assumed in asset acquisition	-	10,541
Proceeds from at-the-market offerings unpaid at period end	-	8,255
Non-cash trade-in of property and equipment	-	200

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 genome 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 genome 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 that targets cells within the body. In parallel, the Company is developing *ex vivo* applications to address immuno-oncology and autoimmune diseases, where the Company uses CRISPR/Cas9 as the tool to create the engineered cell therapy. 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, 2022.

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 equity-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, 2023, the Company has raised an aggregate of \$2,424.1 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, 2023 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, 2022. There have been no material changes to these policies during the nine months ended September 30, 2023.

3. Marketable Securities

The following table summarizes the Company's available-for-sale marketable securities as of September 30, 2023 and December 31, 2022 at net book value:

	September 30, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
(In thousands)				
Marketable securities:				
U.S. Treasury and other government-backed securities	\$ 330,875	\$ 3	\$ (935)	\$ 329,943
Financial institution debt securities	319,226	40	(688)	318,578
Corporate debt securities	115,344	4	(306)	115,042
Other asset-backed securities	61,188	-	(238)	60,950
Total	<u>\$ 826,633</u>	<u>\$ 47</u>	<u>\$ (2,167)</u>	<u>\$ 824,513</u>
	December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
(In thousands)				
Marketable securities:				
U.S. Treasury and other government-backed securities	\$ 244,562	\$ 62	\$ (1,938)	\$ 242,686
Financial institution debt securities	380,891	-	(1,030)	379,861
Corporate debt securities	102,059	-	(509)	101,550
Other asset-backed securities	14,703	-	(346)	14,357
Total	<u>\$ 742,215</u>	<u>\$ 62</u>	<u>\$ (3,823)</u>	<u>\$ 738,454</u>

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At September 30, 2023 and December 31, 2022, the balance in the Company's accumulated other comprehensive loss was composed of activity related to the Company's available-for-sale marketable securities and equity method investment. There were no material realized gains or losses in the nine months ended September 30, 2023 or for the year ended December 31, 2022; therefore, the Company did not reclassify any amounts out of accumulated other comprehensive loss during this period. 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, 2023 and December 31, 2022, the Company did not hold any investments 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.

As of September 30, 2023 and December 31, 2022, the Company's financial assets recognized at fair value on a recurring basis consisted of the following:

	Fair Value as of September 30, 2023			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Assets				
Cash equivalents and restricted cash equivalents	\$ 139,880	\$ 139,880	\$ -	\$ -
Marketable securities:				
U.S. Treasury and other government-backed securities	329,943	77,781	252,162	-
Financial institution debt securities	318,578	-	318,578	-
Corporate debt securities	115,042	-	115,042	-
Other asset-backed securities	60,950	-	60,950	-
Total marketable securities	824,513	77,781	746,732	-
Total Assets	\$ 964,393	\$ 217,661	\$ 746,732	\$ -

	Fair Value as of December 31, 2022			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Assets				
Cash equivalents and restricted cash equivalents	\$ 534,581	\$ 534,581	\$ -	\$ -
Marketable securities:				
U.S. Treasury and other government-backed securities	242,686	172,939	69,747	-
Financial institution debt securities	379,861	-	379,861	-
Corporate debt securities	101,550	-	101,550	-
Other asset-backed securities	14,357	-	14,357	-
Total marketable securities	738,454	172,939	565,515	-
Total Assets	\$ 1,273,035	\$ 707,520	\$ 565,515	\$ -

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.

As discussed further in Note 9, under the Rewrite Merger Agreement, the Rewrite Holders received a \$25.0 million research milestone payment in February of 2023, paid in a combination of \$0.9 million in cash and the remainder in the Company's common stock. The milestone payable in the Company's common stock resulted in liability classification under ASC 480, *Distinguishing Liabilities from Equity* ("ASC 480"). This contingent consideration liability was carried at fair value which was estimated by applying a probability-based model, which utilized inputs based on timing of achievement that were unobservable in the market. The contingent consideration liability was classified within Level 3 of the fair value hierarchy until it was settled in February of 2023.

The following table reconciles the change in fair value of the contingent consideration liability based on the level 3 inputs listed below (in thousands):

	For the Nine Months Ended September 30, 2023	
Balance at December 31, 2022	\$	24,026
Change in fair value		100
Payment of contingent consideration		(24,126)
Balance at September 30, 2023	\$	-

	December 31, 2022	
Discount rate		10.1%
Probability of achievement		100%
Projected year of achievement		2023

5. Accrued Expenses

Accrued expenses consisted of the following:

	September 30, 2023	December 31, 2022
	(In thousands)	
Accrued research and development	\$ 24,241	\$ 32,684
Employee compensation and benefits	21,006	21,778
Accrued legal and professional expenses	1,649	1,457
Accrued other	11,083	4,957
Total accrued expenses	<u>\$ 57,979</u>	<u>\$ 60,876</u>

6. Commitments and Contingencies

Litigation

There have been no material changes to any outstanding litigation, nor is the Company a party to any new litigation, since December 31, 2022. For further information please see the notes to the consolidated financial statements included in the Company's Annual Report for the year ended December 31, 2022.

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, 2023, 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, 2023, the Company's accounts receivable were related to its collaborations with Regeneron Pharmaceuticals, Inc. ("Regeneron"), SparingVision SAS ("SparingVision"), Kyverna Therapeutics, Inc. ("Kyverna"), AvenCell Therapeutics, Inc. ("AvenCell") and ONK Therapeutics, Ltd. ("ONK"), and the Company's contract liabilities were related to its collaborations with Regeneron and SparingVision. As of December 31, 2022, the Company's accounts receivable were related to its collaborations with Regeneron, AvenCell, SparingVision and ONK, and the Company's contract liabilities were related to its collaborations with Regeneron, AvenCell, SparingVision and Kyverna.

The following table presents changes in the Company's accounts receivable and contract liabilities during the nine months ended September 30, 2023 and 2022 (in thousands):

	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

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Nine Months Ended September 30, 2022				
Accounts receivable	\$ 2,031	\$ 8,678	\$ (6,686)	\$ 4,023
Contract liabilities - deferred revenue	\$ 127,235	\$ -	\$ (46,739)	\$ 80,496

During the nine months ended September 30, 2023 and 2022, the Company recognized the following revenues as a result of changes in the contract liability balance (in thousands):

Revenue recognized in the period from:	Nine Months Ended September 30,	
	2023	2022
Amounts included in the contract liability at the beginning of the period	\$ 31,081	\$ 38,208

Costs to obtain and fulfill a contract

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.

License and Collaboration Agreement

In April 2016, the Company entered into a license and collaboration agreement with Regeneron (as amended from time to time, the "2016 Regeneron Agreement"). The 2016 Regeneron Agreement has two principal components: i) a product development component under which the parties will research, develop and commercialize CRISPR/Cas-based therapeutic products primarily focused on genome editing in the liver, and ii) a technology collaboration component, pursuant to which the Company and Regeneron will engage in research-related activities aimed at discovering and developing novel technologies and improvements to CRISPR/Cas technology to enhance the Company's genome editing platform. Under this agreement, the Company also may access the Regeneron Genetics Center and proprietary mouse models to be provided by Regeneron for a limited number of the Company's liver programs. At the inception of the 2016 Regeneron Agreement, Regeneron selected the first of its 10 targets, transthyretin ("ATTR") amyloidosis, which is subject to a co-development and co-promotion agreement between the Company and Regeneron (the "ATTR Co/Co").

In May 2020, the Company entered into (i) amendment no. 1 (the "2020 Regeneron Amendment") to the 2016 Regeneron Agreement, (ii) co-development and co-funding agreements for the treatment of hemophilia A and hemophilia B (the "Hemophilia Co/Co") agreements and (iii) a stock purchase agreement. The collaboration expansion builds upon the jointly developed targeted transgene insertion capabilities designed to durably restore missing therapeutic protein, and to overcome the limitations of traditional gene therapy. The technology collaboration was extended until April 2024, at which point Regeneron would have an option to renew for an additional two years. The 2020 Regeneron Amendment also granted Regeneron exclusive rights to develop products for five additional *in vivo* CRISPR/Cas-based therapeutic liver targets and non-exclusive rights to independently develop and commercialize up to 10 *ex vivo* gene edited products made using certain defined cell types. In October 2023, Regeneron notified the Company that it was exercising 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 million due 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. The collaboration will leverage Intellia's proprietary Nme2 CRISPR/Cas9 genome editing systems adapted for viral vector delivery

and designed to precisely modify a target gene and Regeneron's proprietary antibody-targeted adeno-associated virus vectors and delivery systems. Under the terms of the expanded research collaboration, the companies will initially research two *in vivo* non-liver targets. Intellia will lead the design of the editing methodology and Regeneron will lead the design of the targeted viral vector delivery approach and the parties will share research costs equally. Each party will have the opportunity to lead potential development and commercialization for one product candidate, and the party that is not leading development and commercialization will have the option to enter into a co-development and co-promotion agreement for the target.

Since December 31, 2022, there have been no material changes to the key terms of the 2016 Regeneron Agreement, ATTR Co/Co or Hemophilia Co/Co (the "Regeneron Agreements"), other than as described above.

Revenue Recognition – Collaboration Revenue. Through September 30, 2023, excluding amounts allocated to Regeneron's purchase of the Company's common stock, the Company recorded \$145.0 million in upfront payments under the Regeneron Agreements and \$46.1 million for research and development services, primarily under the ATTR Co/Co agreement. Through September 30, 2023, the Company has recognized \$196.5 million of collaboration revenue under all arrangements, including \$9.3 million and \$23.5 million during the three and nine months ended September 30, 2023, respectively, and \$6.5 million and \$18.6 million during the three and nine months ended September 30, 2022, respectively, in the condensed consolidated statements of operations and comprehensive loss. This includes \$5.5 million and \$14.2 million during the three and nine months ended September 30, 2023 and \$4.0 million and \$8.7 million during the three and nine months ended September 30, 2022, respectively, primarily representing payments due from Regeneron pursuant to the ATTR Co/Co agreement. These revenues are offset in part by contra-revenue related to the Hemophilia Co/Co agreements amounting to approximately \$1.8 million and \$7.6 million during the three and nine months ended September 30, 2023 and \$3.2 million and \$6.9 million during the three and nine months ended September 30, 2022, respectively.

As of September 30, 2023, there was approximately \$12.0 million of the aggregate transaction price remaining to be recognized, which the Company has been recognizing through April 2024 in accordance with the terms of the 2020 Regeneron Amendment.

As of September 30, 2023 and December 31, 2022, the Company had accounts receivable of \$5.5 million and \$3.2 million, respectively, and deferred revenue of \$12.0 million and \$28.8 million, respectively, related to Regeneron Agreements.

AvenCell Therapeutics, Inc.

In July 2021, the Company entered into two agreements with AvenCell, a privately held chimeric antigen receptor T ("CAR-T") cell therapy company formed on that date in a joint venture between the Company, Cellex Cell Professionals GmbH ("Cellex") and funds managed by Blackstone Life Sciences Advisors L.L.C. ("Bxls"): (i) a license and collaboration agreement (the "AvenCell LCA"), under which the Company will collaborate to develop allogeneic universal CAR-T cell therapies and which granted AvenCell a license to develop and commercialize genome edited universal CAR-T cell therapies (limited to its use with their switchable, universal CAR-T cell UniCAR and RevCAR platforms); and (ii) a co-development and co-funding agreement (the "AvenCell Co/Co"), under which the Company would co-develop and co-commercialize allogeneic universal CAR-T cell products for an immuno-oncology indication.

In November 2022, the Company decided to re-prioritize its *ex vivo* programs and terminated the AvenCell Co/Co, effectively turning over control of the program to AvenCell. The Company's obligations under the terminated agreement were completed in the second quarter of 2023. The Company also has one option to enter into an additional co-development and co-funding agreement for a payment of \$30.0 million to AvenCell. Since December 31, 2022, there have been no other material changes to the key terms of the AvenCell LCA and AvenCell Co/Co agreements.

Revenue Recognition – Collaboration Revenue. The Company recognized \$1.9 million and \$13.2 million in revenue related to the AvenCell LCA for the three and nine months ended September 30, 2023, respectively, after eliminating \$1.0 million and \$6.6 million during those respective periods in intra-entity profits, which will be deferred and recognized if and when AvenCell commercializes a product with the Company's license or abandons the related project. Until such time, this revenue is indefinitely deferred and excluded from the results of operations of the Company. The Company recognized no revenue in the three months ended September 30, 2023 and \$0.6 million in contra-revenue in the nine months ended September 30, 2023 related to the AvenCell Co/Co agreement. The Company recognized \$1.3 million and \$1.4 million in contra-revenue in the three and nine months ended September 30, 2022, respectively, related to the AvenCell Co/Co agreement.

As of September 30, 2023, there was no remaining transaction price of the AvenCell LCA remaining to be recognized.

The Company had \$9.0 thousand in accounts receivable and no deferred revenue related to the AvenCell agreements as of September 30, 2023. As of December 31, 2022, the Company had \$0.3 million in accounts receivable and deferred revenue of \$19.9 million related to the AvenCell 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, 2022, there have been no material changes to the key terms of the SparingVision LCA agreement.

Revenue Recognition – Collaboration Revenue. The Company recognized \$0.4 million and \$1.3 million in revenue related to the SparingVision LCA for the three and nine months ended September 30, 2023, respectively. The Company did not recognize collaboration revenue in the three and nine months ended September 30, 2022 related to the SparingVision LCA. As of September 30, 2023 and December 31, 2022, the Company had \$0.7 million and \$0.1 million in accounts receivable, respectively, related to the SparingVision LCA. As of September 30, 2023 and December 31, 2022, the Company had deferred revenue of \$14.1 million and \$14.7 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.

Kyverna Therapeutics, Inc.

In December 2021, the Company and Kyverna, a cell therapy company engineering a new class of therapies for autoimmune and inflammatory diseases, entered into a license and collaboration agreement (the “Kyverna LCA”), for the development of an allogeneic CD19 CAR-T cell therapy for the treatment of a variety of B cell-mediated autoimmune diseases.

Since December 31, 2022, there have been no material changes to the key terms of the Kyverna LCA agreement.

Revenue Recognition – Collaboration Revenue. The Company had recognized revenue from the Kyverna LCA in full as of March 31, 2023, including \$0.4 million in revenue recorded in 2023. The Company recognized approximately \$0.1 million in revenue in the three and nine months ended September 30, 2023 related to materials shipped to Kyverna. The Company recognized \$2.3 million and \$4.3 million in collaboration revenue for the three and nine months ended September 30, 2022, respectively, related to the Kyverna LCA. As of September 30, 2023, the Company had \$0.1 million in accounts receivable related to the shipments made to Kyverna. As of December 31, 2022, the Company had no accounts receivable and deferred revenue of \$0.4 million related to Kyverna.

ONK Therapeutics, Ltd.

On February 12, 2022, the Company entered into a license, collaboration and option agreement (the “ONK LCA”) with ONK, an innovative company dedicated to developing optimally engineered natural killer (“NK”) cell therapies to cure patients with cancer.

Since December 31, 2022, there have been no material changes to the key terms of the ONK LCA agreement.

Revenue Recognition – Collaboration Revenue. The Company recognized \$0.2 million in revenue for each of the three and nine month periods ended September 30, 2023 related to materials shipped in accordance with the ONK LCA. There was no revenue recognized in the three and nine months ended September 30, 2022 related to the ONK LCA. The Company had \$0.2 million and \$0.1 million in accounts receivable related to the ONK LCA at September 30, 2023 and December 31, 2022, respectively.

8. Equity-Method Investment and Other Investments

AvenCell Therapeutics, Inc.

On July 30, 2021, the Company finalized a transaction in which the Company, Cellex and BXLS established AvenCell, a joint venture and privately held company. In exchange for contributing an exclusive license to the joint venture, the Company entered into a Preferred Stock Purchase Agreement with AvenCell for a 33.33% equity interest in AvenCell at the time of the initial closing. Cellex and BXLS each equally owned the remaining 66.67% at that time.

The Company has significant influence over, but does not control, AvenCell through its noncontrolling representation on AvenCell's board of directors and the Company's equity interest in AvenCell. The Company has determined that the preferred stock it owns is in-substance common stock. The Company is not the primary beneficiary as it does not have the power to direct the activities of AvenCell that most significantly impact AvenCell's economic performance. Accordingly, the Company accounts for its investment using the equity method of accounting.

The Company recorded the initial investment in AvenCell of \$62.9 million in "Equity method investments" on its condensed consolidated balance sheet. Due to the timing and availability of AvenCell's financial information, the Company records its share of losses from AvenCell on a quarterly basis on a one-quarter lag. Accordingly, during the third quarter of 2023, the Company recorded its share of the three months of AvenCell's losses generated in the second quarter of 2023 in the Company's operating results and other comprehensive loss. These adjustments resulted in a reduction of the Company's investment by \$3.7 million and \$8.7 million for the three and nine months ended September 30, 2023, respectively. The elimination of the intra-entity profit component of \$1.0 million and \$6.6 million (see Note 7) in the three and nine months ended September 30, 2023, respectively, resulted in a further reduction in the balance of the investment in AvenCell, bringing the carrying value of the investment to \$17.2 million as of September 30, 2023. The Company is not aware of any material events or transactions during the quarter ended September 30, 2023 that would warrant additional disclosure or recognition in the financial statements.

At September 30, 2023, the maximum exposure to loss is limited to the Company's equity investment in the joint venture.

SparingVision SAS

In connection with the SparingVision LCA (see Note 7), the Company received 83,316 shares of SparingVision Series A2 Preferred Stock ("Series A2"). Attached to each share of Series A2, the Company received three warrants for the right to purchase additional Series A2 shares at designated prices that are subject to certain vesting conditions (collectively referred to as the "SparingVision investments"). The Company accounts for the SparingVision investments using the measurement alternative as SparingVision is a private company and there is no readily observable transaction price. The Company recorded the initial investment in SparingVision of \$14.8 million in "Investments and other assets" on its condensed consolidated balance sheet. There was no change in the observable price or impairment of the SparingVision investment as of September 30, 2023.

Kyverna Therapeutics, Inc.

In connection with the Kyverna LCA (see Note 7), the Company received 3,739,515 shares of Kyverna Series B Preferred Stock ("Series B") with a fair value of \$7.0 million. The Company separately made an additional investment in Kyverna, purchasing 1,602,649 shares of Series B in exchange for \$3.0 million in cash (collectively referred to as the "Kyverna investments"). The Company accounts for the Kyverna investments using the measurement alternative as Kyverna is a private company and there is no readily observable transaction price. The Company recorded the initial investment in Kyverna of \$10.0 million in "Investments and other assets" on its condensed consolidated balance sheet. There was no change in the observable price or impairment of the Kyverna investment as of September 30, 2023.

9. Rewrite Acquisition

On February 2, 2022, the Company entered into an Agreement and Plan of Merger by and among the Company, Rewrite Therapeutics, Inc. ("Rewrite"), RW Acquisition Corp. and Shareholder Representative Services, LLC as Securityholder representative (the "Rewrite Merger Agreement"). Under the Rewrite Merger Agreement, the Company paid Company Securityholders (as defined in the Rewrite Merger Agreement) (the "Rewrite Holders") upfront consideration in an aggregate amount of \$45.0 million, excluding customary purchase price adjustments and closing costs, payable in cash. Pursuant to the Rewrite Merger Agreement, the Company acquired all of the issued and outstanding shares of Rewrite. The Rewrite transaction resulted in the acquisition of certain know-how and IP assets related to Rewrite's proprietary DNA writing technology. The Company's management determined that the acquired assets do not meet the definition of a business pursuant to ASC 805, *Business Combinations*, as substantially all of the fair value of the acquired assets is concentrated into one identifiable asset, the DNA writing technology. As of the date of closing of the transactions contemplated by the Rewrite Merger Agreement (the "Rewrite Merger Agreement Date"), the asset acquired had no alternative future use and had not reached a stage of technological feasibility. As a result, all payment obligations were recorded as research and development expense in the condensed consolidated statements of operations and other comprehensive loss in the amount of \$56.0 million. The total transaction price was allocated to the assets acquired and liabilities assumed on a relative fair value basis.

In addition, the Rewrite Holders are eligible to receive up to an additional \$155.0 million, including \$55.0 million upon the achievement of pre-specified research milestones and \$100.0 million upon the achievement of a regulatory approval milestone, payable through a mixture of \$130.0 million in cash and \$25.0 million in a combination of cash and the Company's common stock which would be valued using the volume-weighted average price of the Company's Common Stock over the ten consecutive trading day period ending on and including the trading day that is two trading days immediately prior to the issuance of the consideration issued in connection with the applicable milestone. In September 2022, Rewrite Therapeutics, Inc. merged into Intellia, with Intellia the surviving entity.

In January 2023, the \$25.0 million research milestone noted above was achieved and, in February 2023, the Company paid the Rewrite Holders \$0.9 million in cash and issued 567,045 shares of Intellia common stock in order to fulfill its obligation under the Rewrite Merger Agreement. The cash obligation was recorded as research and development expense in the condensed consolidated statement of operations and other comprehensive loss in the first quarter of 2023. The Company had determined that the research milestone settled in the Company's common stock would be classified as a contingent consideration liability under ASC 480 and, therefore, the Company initially recorded a liability for this milestone payment as of the Rewrite Merger Agreement Date at its original fair value of \$10.5 million. The contingent consideration liability was remeasured at fair value each financial reporting period, with the resulting impact reflected in the Company's condensed consolidated statements of operations and other comprehensive loss, presented within other income (expense). The remaining milestones to be settled in cash would be recorded when the contingency is resolved and the consideration is paid or becomes payable.

The transaction price on the Rewrite Merger Agreement Date was determined and allocated as follows (in thousands):

Transaction Price

Upfront cash consideration	\$	43,730
Research contingent consideration liabilities		10,541
Transaction costs		1,838
Total transaction price	\$	<u>56,109</u>

Transaction Price Allocated

In-process research and development	\$	55,990
Cash acquired		287
Other current assets acquired		153
Other liabilities assumed		<u>(321)</u>
Total transaction price	\$	<u>56,109</u>

10. Leases

In January 2023, the Company performed a remeasurement of their lease for office and laboratory space located at 640 Memorial Drive, Cambridge, Massachusetts, as the Company's rentable square footage had been modified. This remeasurement included an update to the incremental borrowing rate from 7.99% to 8.4%, and resulted in a decrease in the right of use asset and lease liability of \$0.2 million.

Also in January 2023, the Company executed a sublease for a portion of their leased office and laboratory space at 730 Main Street, Cambridge, Massachusetts.

In February 2022, the Company entered into an agreement to lease approximately 140,000 square feet of manufacturing space located at 840 Winter Street, Waltham, Massachusetts (the "840 Winter Lease"), which will provide the Company with the ability to manufacture its own products in a good manufacturing practice ("GMP") compliant facility as well as to supplement the Company's current leased premises in Cambridge, Massachusetts. The 840 Winter Lease, including the obligation to pay rent, is expected to commence in 2024 for an initial term of twelve years. The base rent under the 840 Winter Lease is \$73.50 per square foot per year during the first year of the term, which is subject to scheduled 3% annual increases, plus certain operating expenses and taxes. The Company has the option to extend the 840 Winter Lease for two five-year terms.

In June 2023, the Company executed an amendment to the 840 Winter Lease, which outlines the Company's and the landlord's responsibilities regarding the construction of the leased space. The Company will be responsible for the oversight of the construction of the tenant improvements, which will be primarily funded by a tenant improvement allowance of \$250 per rentable square foot. The Company has elected an additional tenant improvement allowance of \$50 per rentable square foot to be repaid over the term of the lease with interest, with an option to increase the allowance by an additional \$100 per rentable square foot

which would also be repaid over the term of the lease with interest. The Company will also be responsible for certain future construction costs to the extent that they exceed the tenant improvement allowance. The Company anticipates a phased move-in process during the second half of 2024. As of September 30, 2023, 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”).

11. Equity-Based Compensation

Equity-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,	
	2023	2022	2023	2022
	(In thousands)			
Research and development	\$ 21,235	\$ 16,383	\$ 60,517	\$ 40,736
General and administrative	14,117	8,832	38,490	26,038
Total	<u>\$ 35,352</u>	<u>\$ 25,215</u>	<u>\$ 99,007</u>	<u>\$ 66,774</u>

Amended and Restated 2015 Stock Option and Incentive Plan

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.

The Company maintains a retirement policy for equity awards granted to all employees (the “Retirement Policy”), which applies to all equity awards granted after July 1, 2022 to employees who meet certain retirement eligibility criteria set forth in the Retirement Policy (the “Retirees”). Pursuant to the terms of the Retirement Policy, upon a Retiree’s eligible retirement: (i) all stock options held by the Retiree will continue to vest following the Retiree’s retirement date according to the original vesting schedule of the option until fully vested and all vested stock options held by such Retiree will remain exercisable until the earlier of the five-year anniversary of the Retiree’s retirement date or the original expiration date of the option, (ii) all unvested time-based RSUs held by the Retiree will vest in full on the Retiree’s retirement date and (iii) all unvested performance-based awards held by the Retiree will remain outstanding following the Retiree’s retirement date and the Retiree will remain eligible to earn a pro-rated portion of such performance-based awards at the end of the performance period based on actual performance during the performance period.

As of September 30, 2023, there were 4,005,307 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.

Restricted Stock Units

The following table summarizes the Company’s RSU activity for the nine months ended September 30, 2023:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Unvested restricted stock units as of December 31, 2022	1,941,379	\$ 70.70
Granted	2,774,271	42.36
Vested	(597,610)	68.31
Cancelled	(193,503)	49.70
Unvested restricted stock units as of September 30, 2023	<u>3,924,537</u>	<u>\$ 52.07</u>

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.

Also in March 2023, 181,743 market-based RSUs were granted to senior executives as part of their annual grant. These RSUs have the potential to vest after a period of three years, with a vesting start date of January 1, 2023, 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 grant date fair value for these RSUs, calculated using a Monte Carlo valuation model, was \$68.55. The following assumptions were used to determine the grant date fair value: risk free interest rate: 4.60%; expected dividend yield: 0.0%; expected volatility: 84.34%; expected term (in years): 2.84.

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, 2023 and, therefore, no related stock-based compensation was recorded during the period then ending.

All RSUs that are not market-based are measured at fair value based on the quoted price of the Company's common stock.

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. The weighted-average grant date fair value of RSUs granted during the three and nine months ended September 30, 2022 was \$55.59 and \$72.48, respectively. The total fair value of RSUs vested (measured on the date of vesting) for the three and nine months ended September 30, 2022 was \$0.1 million and \$8.0 million, respectively.

As of September 30, 2023, there was \$143.2 million of unrecognized equity-based compensation expense related to RSUs that are expected to vest; these costs are expected to be recognized over a weighted average remaining vesting period of 1.86 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 \$28.92 and \$57.23 per option for those options granted during the nine months ended September 30, 2023 and 2022, respectively. There were no options granted during the three months ended September 30, 2023 and 2022. 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, 2023 was \$4.8 million and \$6.6 million, respectively, and during the three and nine months ended September 30, 2022 was \$1.4 million and \$41.8 million, respectively. Weighted average assumptions used to apply this pricing model were as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Risk-free interest rate	n/a	n/a	4.4%	1.9%
Expected life of options	n/a	n/a	6.0 years	5.9 years
Expected volatility of underlying stock	n/a	n/a	78.7%	76.2%
Expected dividend yield	n/a	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. The expected volatility was derived from a blend of the Company's historical volatility and an average of the historical stock volatilities of several peer companies within the Company's industry, both over a period equivalent to the expected term of the stock option grants.

Expected Dividend Yield. The expected dividend yield assumption is based on the fact that the Company has never paid cash dividends and has no present intention to pay cash dividends.

Stock options granted under the 2015 Plan in 2023 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 performance-based vesting provisions. The maximum term of stock options granted under the 2015 Plan is ten years.

The Company uses the market closing price of its common stock as reported on the Nasdaq Global Select Market to determine the fair value of the shares of common stock underlying stock options.

The following is a summary of stock option activity for the nine months ended September 30, 2023:

	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, 2022	5,471,675	\$ 49.86		
Granted	569,821	41.00		
Exercised	(319,847)	17.52		
Forfeited	(130,474)	80.20		
Outstanding at September 30, 2023	<u>5,591,175</u>	\$ 50.10	6.87	\$ 39,821
Exercisable at September 30, 2023	<u>3,846,015</u>	\$ 42.52	6.30	\$ 36,370

As of September 30, 2023, there was \$69.2 million of unrecognized compensation cost related to stock options that have not yet vested; these costs are expected to be recognized over a weighted average remaining vesting period of 1.63 years.

2016 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, 2023, there were 1,149,953 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, 2023 and 2022 the Company issued 69,631 and 24,316 shares of common stock under the 2016 Plan, respectively. The weighted-average purchase prices of shares issued under the 2016 Plan were \$29.45 and \$44.00 per share for the nine-month periods ended September 30, 2023 and 2022, 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,	
	2023	2022	2023	2022
Risk-free interest rate	5.53%	2.52%	4.7%-5.53%	0.22%-2.52%
Expected term (in years)	0.5 years	0.5 years	0.5 years	0.5 years
Expected volatility of underlying stock	60.4%	95.3%	60.4%-69.2%	63.6%-95.3%
Expected dividend yield	0.0%	0.0%	0.0%	0.0%

12. 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,	
	2023	2022	2023	2022
	(In thousands)			
Net loss	\$ (122,224)	\$ (113,229)	\$ (349,031)	\$ (360,779)
Weighted average shares outstanding, basic and diluted	88,645	76,047	88,204	75,543
Net loss per share, basic and diluted	<u>\$ (1.38)</u>	<u>\$ (1.49)</u>	<u>\$ (3.96)</u>	<u>\$ (4.78)</u>

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,	
	2023	2022
	(In thousands)	
Unvested restricted stock units	3,925	1,928
Stock options	5,591	5,548
	<u>9,516</u>	<u>7,476</u>

13. Stockholders' Equity

The following tables present changes in stockholders' equity for the nine-month periods ended September 30, 2023 and 2022 (in thousands, except share data):

	Common		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
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	-	-	-	-	-
Equity-based compensation	-	-	27,255	-	-	27,255
Other comprehensive loss - unrealized gain on marketable securities	-	-	-	2,989	-	2,989
Other comprehensive loss - 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
Equity-based compensation	-	-	36,400	-	-	36,400
Other comprehensive loss - unrealized loss on marketable securities	-	-	-	(1,482)	-	(1,482)
Other comprehensive loss - 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 loss - unrealized gain on marketable securities	-	-	-	142	-	142
Other comprehensive loss - 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

	Common		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2021	74,485,883	\$ 7	\$ 1,745,870	\$ (2,632)	\$ (703,001)	\$ 1,040,244
Issuance of common stock through at-the-market offerings, net of issuance costs of \$164	579,788	1	38,885	-	-	38,886
Exercise of stock options	503,830	-	8,435	-	-	8,435
Vesting of restricted stock units	54,666	-	-	-	-	-
Equity-based compensation	-	-	18,491	-	-	18,491
Other comprehensive loss - unrealized loss on marketable securities	-	-	-	(5,128)	-	(5,128)
Other comprehensive loss - equity method investment	-	-	-	(302)	-	(302)
Net loss	-	-	-	-	(146,872)	(146,872)
Balance at March 31, 2022	75,624,167	8	1,811,681	(8,062)	(849,873)	953,754
Exercise of stock options	315,747	-	4,827	-	-	4,827
Vesting of restricted stock units	36,515	-	-	-	-	-
Issuance of shares under employee stock purchase plan	24,316	-	1,068	-	-	1,068
Equity-based compensation	-	-	23,068	-	-	23,068
Other comprehensive loss - unrealized loss on marketable securities	-	-	-	(932)	-	(932)
Other comprehensive loss - equity method investment	-	-	-	(560)	-	(560)
Net loss	-	-	-	-	(100,678)	(100,678)
Balance at June 30, 2022	76,000,745	8	1,840,644	(9,554)	(950,551)	880,547
Issuance of common stock through at-the-market offerings, net of issuance costs of \$54	553,204	-	31,510	-	-	31,510
Exercise of stock options	33,336	-	722	-	-	722
Vesting of restricted stock units	662	-	-	-	-	-
Equity-based compensation	-	-	25,215	-	-	25,215
Other comprehensive loss - unrealized gain on marketable securities	-	-	-	991	-	991
Other comprehensive loss - equity method investment	-	-	-	(805)	-	(805)
Net loss	-	-	-	-	(113,229)	(113,229)
Balance at September 30, 2022	76,587,947	\$ 8	\$ 1,898,091	\$ (9,368)	\$ (1,063,780)	\$ 824,951

At-the-Market Offering Programs

2019 Sale Agreement

In August 2019, the Company entered into an Open Market Sale Agreement (the "2019 Sale Agreement") with Jefferies LLC ("Jefferies"), under which Jefferies was able to offer and sell, from time to time in "at-the-market" offerings, common stock having aggregate gross proceeds of up to \$150.0 million. The Company agreed to pay Jefferies cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2019 Sale Agreement. Under the 2019 Sale Agreement, the Company issued 3,778,889 shares of its common stock.

During the first quarter of 2022, the Company issued 579,788 shares of its common stock, in a series of sales, at an average price of \$69.43 per share, in accordance with the 2019 Sale Agreement for aggregate net proceeds of \$38.9 million, after payment of cash commissions to Jefferies and approximately \$0.2 million related to legal, accounting and other fees in connection with the sales. The 2019 Sale Agreement expired in the third quarter of 2022.

2022 Sale Agreement

In March 2022, the Company entered into an Open Market Sale Agreement (the “2022 Sale Agreement”) with Jefferies, under which Jefferies is 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. The Company agreed to pay Jefferies cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2022 Sale Agreement. Through September 30, 2023, the Company issued 3,836,020 shares of its common stock under the 2022 Sale Agreement.

During the nine months ended September 30, 2023, the Company issued 440,681 shares of its common stock, in a series of sales, at an average price of \$38.20 per share, in accordance with the 2022 Sale Agreement for aggregate net proceeds of \$16.2 million, after payment of cash commissions to Jefferies and approximately \$0.1 million related to legal, accounting and other fees in connection with the sales.

During the nine months ended September 30, 2022, the Company issued 553,204 shares of its common stock, in a series of sales, at an average price of \$58.82 per share, in accordance with the 2022 Sale Agreement for aggregate net proceeds of \$31.5 million, after payment of cash commissions to Jefferies and approximately \$0.1 million related to legal, accounting and other fees in connection with the sales. As of September 30, 2022, \$8.3 million of these proceeds were recorded as an other current asset on the Company’s condensed consolidated balance sheet, representing offerings with trade dates in September 2022 that were settled in October 2022.

As of September 30, 2023, \$188.2 million in shares of common stock remain eligible for sale under the 2022 Sale Agreement.

Approval of Additional Authorized Shares

In June 2023, the Company filed a Certificate of Amendment to the Company’s Second Amended and Restated Certificate of Incorporation to increase the number of authorized shares of common stock from 120,000,000 to 240,000,000. The increase in the number of authorized shares was approved by the holders of a majority of the outstanding shares of the Company’s common stock at its Annual Meeting of Stockholders held on June 14, 2023.

14. Related Party Transactions

In the ordinary course of business, the Company may purchase materials or supplies from entities that are associated with a party that meets the criteria of a related party of the Company. These transactions are reviewed quarterly and to date have not been material to the Company’s condensed consolidated financial statements.

The Company and AvenCell are parties to the AvenCell LCA and AvenCell Co/Co, as described in Note 7. The Company’s relationship with AvenCell is considered to be as a related party due to the Company’s 33.33% investment in AvenCell being accounted for under the equity method. The Company recognized \$1.9 million and \$13.2 million in revenue related to the AvenCell LCA for the three and nine months ended September 30, 2023, respectively, after eliminating \$1.0 million and \$6.6 million during those respective periods in intra-entity profits, which will be deferred and recognized if and when AvenCell commercializes a product with the Company’s license or abandons the related project. Until such time, this revenue is indefinitely deferred and excluded from the results of operations of the Company. The Company recognized no revenue in the three months ended September 30, 2023 and \$0.6 million in contra-revenue in the nine months ended September 30, 2023 related to the AvenCell Co/Co agreement. The Company recognized \$1.3 million in revenue and \$1.4 million in contra-revenue in the three and nine months ended September 30, 2022, respectively, related to the AvenCell Co/Co agreement. As of September 30, 2023 the Company had recognized all revenue related to the AvenCell LCA.

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 initiate and complete our Phase 3 study, 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 Phase 1/2 study, determine a recommended dose that can be advanced into later-stage studies and initiate our Phase 3 study, or the success of such program;
- the anticipated timing of our clinical trial application ("CTA") filing for NTLA-3001, our program for the treatment of alpha-1 antitrypsin deficiency ("AATD")-associated lung disease, or the success of such program;
- our ability to successfully execute our development plans for our preclinical programs, including NTLA-3001;
- 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;
- the scope of protection we are able to develop, establish and maintain for intellectual property rights, including patents 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 genome 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 genome 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 that targets cells within the body. In parallel, we are developing *ex vivo* applications to address immuno-oncology and autoimmune diseases, where we use CRISPR/Cas9 as the tool to create the engineered cell therapy. 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, 2022.

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 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 genome 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, 2023, we have raised an aggregate of approximately \$2,424.1 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 parallel, 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 is the first investigational CRISPR-based therapy to be systemically delivered to edit genes inside the human body and has the potential to be the first single-dose treatment for ATTR amyloidosis. Delivered with our *in vivo* LNP technology, NTLA-2001 offers the possibility of halting and reversing the disease by driving a deep, consistent and potentially lifelong reduction in transthyretin (“TTR”) protein after a single dose.

The Phase 1 study of NTLA-2001 is a two-part, open-label study in adults with ATTR amyloidosis with cardiomyopathy (“ATTR-CM”) or hereditary ATTR amyloidosis with polyneuropathy (“ATTRv-PN”). In November, we announced new positive interim results from the Phase 1 study of NTLA-2001. Updated data from over 60 patients showed consistent, deep, and durable serum TTR reduction achieved with a single dose of NTLA-2001, including in 29 patients who reached 12 months or more of follow-up as of the data cutoff date of May 11, 2023. Across all patients who received a dose of 0.3 mg/kg or higher (n=62), the median serum TTR reduction was 91% and the median absolute residual serum TTR concentration was 17 ug/mL at day 28. Across all patients and at all dose levels tested, NTLA-2001 was generally well tolerated, and the majority of adverse events were mild in severity. These interim data were presented at the 4th International ATTR Amyloidosis Meeting, held in Madrid, Spain.

In October 2023, we announced that the U.S. Food and Drug Administration (“FDA”) cleared the NTLA-2001 Phase 3 investigational new drug (“IND”) application for the treatment of ATTR-CM. The MAGNITUDE pivotal Phase 3 study is a randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of NTLA-2001 in approximately 765 patients with ATTR-CM. The primary endpoint of the study is a composite endpoint of cardiovascular (“CV”)-related mortality and CV-related events. Patients will be randomized 2:1 NTLA-2001:placebo, with a single 55 mg infusion of NTLA-2001 administered. The MAGNITUDE study is expected to initiate by year-end with patient dosing to commence early 2024.

We are actively preparing for a global pivotal Phase 3 study of NTLA-2001 for the treatment of ATTRv-PN, which includes discussions with regulatory authorities.

NTLA-2001 is the subject of a co-development and co-promotion (“Co/Co”) agreement directed to our first collaboration target 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 our wholly owned candidate for the treatment of HAE. NTLA-2002 is designed to knock out the *kallikrein B1* (“*KLKB1*”) gene in the liver, with the potential to permanently reduce total plasma kallikrein protein and activity, a key mediator of HAE. This investigational approach aims to prevent attacks for people living with HAE by providing continuous reduction of plasma kallikrein activity, following a single dose. It also aims to eliminate the significant treatment burden associated with currently available HAE therapies.

NTLA-2002 is being evaluated in a Phase 1/2 study in adults with Type I or Type II HAE.

In June 2023, we announced additional positive interim results from the Phase 1 portion of the ongoing Phase 1/2 study of NTLA-2002 at the European Academy of Allergy and Clinical Immunology Hybrid Congress. Across all ten patients, a 95% mean reduction in monthly attack rate was observed after a single dose of NTLA-2002 through the latest follow-up. The median duration of follow-up was 9.0 months (range of 5.6 - 14.1 months). At all three dose levels evaluated, NTLA-2002 has been well tolerated, and the majority of adverse events were mild in severity.

In March 2023, we announced that the FDA cleared our NTLA-2002 IND application, enabling the company to include the U.S. in the global Phase 2. In August 2023, we announced that due to the substantial interest from physicians and patients to participate in the NTLA-2002 clinical program, all patients have been identified for the Phase 2 portion of the study with enrollment expected to be completed in the fourth quarter of 2023. Additionally, we announced that following the March 2023 IND clearance, the FDA requested supplemental preclinical data related to the inclusion of female patients of child-bearing potential. We are on track to complete the additional mouse study in the first half of next year and expect to submit these data in advance of the planned Phase 3 trial, which will complement the clinical data collected from female patients of child-bearing potential dosed in the ongoing Phase 1/2 study.

We plan to initiate the global pivotal Phase 3 study, including U.S. patients, as early as the third quarter of 2024, subject to regulatory feedback.

In October 2023, we announced that the European Medicines Agency (“EMA”) granted Priority Medicine (“PRIME”) designation to NTLA-2002 for the treatment of HAE. PRIME designation is granted by the EMA to drug candidates that may offer a major therapeutic advantage over existing treatments or that benefit patients without treatment options. PRIME is the fourth specialty regulatory designation we have received for NTLA-2002. NTLA-2002 was also granted Orphan Drug Designation and Regenerative Medicine Advanced Therapy (“RMAT”) Designation by the FDA, as well as the Innovation Passport by the U.K. Medicines and Healthcare products Regulatory Agency (“MHRA”).

Alpha-1 Antitrypsin Deficiency (“AATD”) Program

NTLA-3001 for associated lung disease:

NTLA-3001 is our wholly owned, first-in-class CRISPR-mediated *in vivo* targeted gene insertion development candidate for the treatment of AATD-associated lung disease. It is designed to precisely insert a healthy copy of the *SERPINA1* gene, which encodes the alpha-1 antitrypsin (“A1AT”) protein, with the potential to restore permanent expression of functional A1AT protein to therapeutic levels after a single dose. Our approach seeks to improve patient outcomes, including eliminating the need for weekly intravenous infusions of A1AT augmentation therapy or lung transplant in severe cases. We plan to submit a Clinical Trial Application (“CTA”) in the first quarter of 2024 to initiate a first-in-human, Phase 1 study of NTLA-3001.

NTLA-2003 for associated liver disease:

NTLA-2003 is our wholly owned, *in vivo* knockout development candidate for the treatment of AATD-associated liver disease. It is designed to inactivate the *SERPINA1* gene responsible for the production of abnormal A1AT protein in the liver. Based on a prioritization of resources, we are making a strategic shift to halt further IND-enabling activities for NTLA-2003 to advance an AATD research-stage program leveraging our DNA writing technology.

In Vivo Research Programs

We continue to work on various liver-focused programs, such as hemophilia A and hemophilia B, which we are co-developing with Regeneron, as well as other liver targets, which we are working on both independently and in partnership with Regeneron, that would leverage our capabilities to knockout, insert and make consecutive edits to the genome.

We are further investigating delivery strategies that target tissues outside of the liver. For example, we have presented preclinical data establishing proof-of-concept for non-viral genome editing of bone marrow and hematopoietic stem cells (“HSCs”) in mice. This represented our first demonstration of systemic *in vivo* genome editing in bone marrow using our proprietary non-viral delivery platform. We believe these results extend our modular *in vivo* capabilities to treat inherited blood disorders such as sickle cell disease. In September 2023, we entered into an expanded research collaboration with Regeneron to develop additional *in vivo* CRISPR-based gene editing therapies focused on neurological and muscular diseases. In addition, we are collaborating with SparingVision SAS (“SparingVision”) to develop novel genomic medicines utilizing CRISPR/Cas9 technology for the treatment of ocular diseases.

Ex Vivo Programs

We are advancing multiple preclinical 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 is designed to avoid both T cell- and natural killer (“NK”) cell-mediated rejection, a key unsolved challenge with other investigational allogeneic approaches.

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, Kyverna Therapeutics, Inc. (“Kyverna”), and ONK Therapeutics, Ltd (“ONK”). 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 collaboration and license 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 equity-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 equity-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

Other income (expense), net consists of interest income earned on our cash, cash equivalents, restricted cash equivalents and marketable securities, loss from 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, 2023 and 2022

The following table summarizes our results of operations for the three months ended September 30, 2023 and 2022:

	Three Months Ended September 30,		Period-to- Period Change
	2023	2022	
	(In thousands)		
Collaboration revenue	\$ 11,992	\$ 13,266	\$ (1,274)
Operating expenses:			
Research and development	113,696	96,651	17,045
General and administrative	29,403	22,145	7,258
Total operating expenses	143,099	118,796	24,303
Operating loss	(131,107)	(105,530)	(25,577)
Other income (expense), net:			
Interest income	12,740	1,945	10,795
Loss from equity method investment	(3,857)	(1,834)	(2,023)
Change in fair value of contingent consideration	-	(7,810)	7,810
Total other income (expense), net	8,883	(7,699)	16,582
Net loss	\$ (122,224)	\$ (113,229)	\$ (8,995)

Collaboration Revenue

Collaboration revenue decreased by \$1.3 million to \$12.0 million during the three months ended September 30, 2023, as compared to \$13.3 million during the three months ended September 30, 2022. The decrease in collaboration revenue during the three months ended September 30, 2023 is primarily due to the Kyverna and AvenCell license and collaboration agreements, as this revenue was recognized in full as of the first and third quarters of 2023, respectively, offset in part by revenue from our license and collaboration agreements with Regeneron and SparingVision. See Note 7, "Collaborations and Other Arrangements" of 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 \$17.0 million to \$113.7 million during the three months ended September 30, 2023, as compared to \$96.7 million during the three months ended September 30, 2022.

The following table summarizes our research and development expenses for the three months ended September 30, 2023 and 2022, 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
	2023	2022		
	(In thousands)			
External development expenses by program:				
NTLA-2001	\$ 16,404	\$ 10,249	\$ 6,155	60 %
NTLA-2002	4,798	2,808	1,990	71 %
NTLA-3001	8,563	2,325	6,238	268 %
NTLA-5001	-	6,531	(6,531)	-100 %
Unallocated research and development expenses:				
Employee-related expenses	32,317	29,897	2,420	8 %
Research materials and contracted services	16,084	18,646	(2,562)	-14 %
Facility-related expenses	13,168	8,946	4,222	47 %
Stock-based compensation	21,235	16,383	4,852	30 %
Other	1,127	866	261	30 %
Total research and development expenses	\$ 113,696	\$ 96,651	\$ 17,045	18 %

The increase in research and development expenses for the three months ended September 30, 2023 compared to the three months ended September 30, 2022 was primarily attributable to:

- a \$6.2 million increase in external costs related to the development of NTLA-2001, primarily due to an increase in spend on contracted services and drug components;
- a \$2.0 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 \$6.2 million increase in external costs related to the development of NTLA-3001, primarily due to an increase in spend on contracted services, drug components and consulting costs;
- a \$6.5 million decrease in external costs related to NTLA-5001, as we continue to wind down the program as part of the pivot to an allogeneic pipeline;
- a \$2.4 million increase in employee-related expenses primarily driven by the increase in personnel growth to support our lead programs;
- a \$2.6 million decrease in research materials and contracted services;
- a \$4.2 million increase in facility-related expenses primarily related to rent, depreciation and technology expense allocated to research and development; and
- a \$4.9 million increase in stock-based compensation driven by our larger workforce.

General and Administrative

General and administrative expenses increased by approximately \$7.3 million to \$29.4 million during the three months ended September 30, 2023, compared to \$22.1 million during the three months ended September 30, 2022. This increase was primarily related to employee-related expenses, including an increase in stock-based compensation of \$5.3 million, driven by our larger workforce.

Other Income (Expense), Net

The increase in other income (expense), net of \$16.6 million is related to a \$10.8 million increase in interest income, driven by an increase in market rates, and a \$7.8 million increase in the change in fair value of contingent consideration, offset in part by a \$2.0 million increase in the loss from our equity method investment.

Comparison of Nine Months Ended September 30, 2023 and 2022

The following table summarizes our results of operations for the nine months ended September 30, 2023 and 2022:

	Nine Months Ended September 30,		Period-to- Period Change
	2023	2022	
	(In thousands)		
Collaboration revenue	\$ 38,192	\$ 38,548	\$ (356)
Operating expenses:			
Research and development	326,088	319,945	6,143
General and administrative	87,503	66,680	20,823
Total operating expenses	413,591	386,625	26,966
Operating loss	(375,399)	(348,077)	(27,322)
Other income (expense), net:			
Interest income	37,373	3,188	34,185
Loss from equity method investment	(10,905)	(7,831)	(3,074)
Change in fair value of contingent consideration	(100)	(8,059)	7,959
Total other income (expense), net	26,368	(12,702)	39,070
Net loss	<u>\$ (349,031)</u>	<u>\$ (360,779)</u>	<u>\$ 11,748</u>

Collaboration Revenue

Collaboration revenue decreased by \$0.4 million to \$38.2 million during the nine months ended September 30, 2023, as compared to \$38.5 million during the nine months ended September 30, 2022. 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 \$6.1 million to \$326.1 million during the nine months ended September 30, 2023, as compared to \$319.9 million during the nine months ended September 30, 2022.

The following table summarizes our research and development expenses for the nine months ended September 30, 2023 and 2022, together with the changes in those items in dollars and the respective percentages of change:

	Nine Months Ended September 30,		Period-to-	Percent
	2023	2022	Period Change	Change
	(In thousands)			
External development expenses by program:				
NTLA-2001	\$ 39,523	\$ 27,838	\$ 11,685	42 %
NTLA-2002	16,408	7,865	8,543	109 %
NTLA-3001	16,724	8,002	8,722	109 %
NTLA-5001	-	16,410	(16,410)	-100 %
Unallocated research and development expenses:				
Employee-related expenses	103,437	83,433	20,004	24 %
Research materials and contracted services	46,003	51,720	(5,717)	-11 %
In-process research and development	-	55,990	(55,990)	-100 %
Rewrite research milestone	874	-	874	-
Facility-related expenses	38,891	25,645	13,246	52 %
Stock-based compensation	60,517	40,736	19,781	49 %
Other	3,711	2,306	1,405	61 %
Total research and development expenses	<u>\$ 326,088</u>	<u>\$ 319,945</u>	<u>\$ 6,143</u>	<u>2 %</u>

The increase in research and development expenses for the nine months ended September 30, 2023 compared to the nine months ended September 30, 2022 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 drug components and contracted services;
- an \$8.5 million increase in external costs related to the development of NTLA-2002, primarily due to an increase in spend on drug components, contracted services and consulting services;
- an \$8.7 million increase in external costs related to NTLA-3001, primarily related to an increase in spend on drug components and consulting and professional services, offset in part by a decrease in spend on contracted services;
- a \$16.4 million decrease in external costs related to the development of NTLA-5001, as we continue to wind down the program as part of the pivot to an allogeneic pipeline;
- a \$20.0 million increase in employee-related expenses, primarily driven by the increase in personnel growth to support our lead programs;
- a \$5.7 million decrease in research materials and contracted services primarily driven by a decrease in drug component expenses and contracted services related to early stage programs;
- a \$56.0 million decrease in in-process research and development expense related to the acquisition of Rewrite Therapeutics, Inc. in the first half of 2022;
- a \$13.2 million increase in facility-related expenses primarily related to rent, depreciation and technology expense allocated to research and development; and
- a \$19.8 million increase in stock-based compensation driven by our larger workforce.

General and Administrative

General and administrative expenses increased by \$20.8 million to \$87.5 million during the nine months ended September 30, 2023, compared to \$66.7 million during the nine months ended September 30, 2022. This increase was primarily related to an increase in employee-related expenses, including stock-based compensation of \$12.5 million, driven by our larger workforce.

Other Income (Expense), Net

The increase in other income (expense), net of \$39.1 million is primarily related to a \$34.2 million increase in interest income, driven by an increase in market rates, and an \$8.0 million increase in the change in fair value of contingent consideration, offset in part by a \$3.1 million increase in the loss from our equity method investment.

Liquidity and Capital Resources

Since our inception through September 30, 2023, we have raised an aggregate of \$2,424.1 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, 2023, we had \$992.5 million in cash, cash equivalents and marketable securities.

We are eligible to earn a significant amount of milestone payments and royalties, in each case, on a per-product basis under our collaborations with Novartis Institutes for BioMedical Research, Inc. (“Novartis”), SparingVision and ONK, on a per-target basis under our collaboration with Regeneron and upon achievement of certain events under our collaboration with Kyverna. Our ability to earn these milestone payments and the timing of achieving these milestones is dependent upon the outcome of our research and development activities and is uncertain at this time. Our rights to payments under our collaboration agreements are our only committed external source of funds.

At-the-Market Offering Programs

2019 Sale Agreement

In August 2019, we entered into an Open Market Sale Agreement (the “2019 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 our common stock having aggregate gross proceeds of up to \$150.0 million. We agreed to pay to Jefferies cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2019 Sale Agreement. Under the 2019 Sale Agreement we issued 3,778,889 shares of our common stock.

During the first quarter of 2022, we issued 579,788 shares of our common stock in a series of sales at an average price of \$69.43 per share in accordance with the 2019 Sale Agreement, for aggregate net proceeds of \$38.9 million after payment of cash commissions to Jefferies and approximately \$0.2 million related to legal, accounting and other fees in connection with the sales. The 2019 Sale Agreement expired in the third quarter of 2022.

2022 Sale Agreement

In March 2022, we entered into an Open Market Sale Agreement (the “2022 Sale Agreement”) with 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. We agreed to pay Jefferies cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2022 Sale Agreement. To date we have issued 3,836,020 shares of our common stock under the 2022 Sale Agreement.

During the nine months ended September 30, 2023, we issued 440,681 shares of our common stock, in a series of sales, at an average price of \$38.20 per share, in accordance with the 2022 Sale Agreement for aggregate net proceeds of \$16.2 million, after payment of cash commissions to Jefferies and approximately \$0.1 million related to legal, accounting and other fees in connection with the sales.

During the nine months ended September 30, 2022, we issued 553,204 shares of our common stock, in a series of sales, at an average price of \$58.82 per share, in accordance with the 2022 Sale Agreement for aggregate net proceeds of \$31.5 million, after payment of cash commissions to Jefferies and approximately \$0.1 million related to legal, accounting and other fees in connection

with the sales. As of September 30, 2022, \$8.3 million of these proceeds were recorded as an other current asset on our condensed consolidated balance sheet, representing offerings with trade dates in September 2022 that were settled in October 2022.

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 2023, we expect our expenses to increase compared to prior periods in connection with our ongoing activities as we continue to grow our research and development team, 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 for the ATTR and hemophilia programs. Additionally, we are eligible to earn milestone payments and royalties, in each case, on a per-product basis under our collaborations with Novartis, SparingVision and ONK, 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, 2023, 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 beyond the next 24 months, 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 for the nine months ended September 30, 2023 and 2022:

	Nine Months Ended September 30,	
	2023	2022
	(In thousands)	
Net cash used in operating activities	\$ (301,032)	\$ (243,418)
Net cash (used in) provided by investing activities	(77,286)	190,461
Net cash provided by financing activities	23,839	77,192

Net cash used in operating activities

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, losses on equity method investment of \$17.5 million and depreciation of \$6.5 million.

Net cash used in operating activities of \$243.4 million during the nine months ended September 30, 2022 primarily consists of a net loss of \$360.8 million, further reduced by changes in operating assets and liabilities of \$40.5 million, including the receipt of \$6.7 million in payments from our collaboration partners during that period and offset in part by non-cash charges of stock-based compensation of \$66.8 million, in-process research and development expense of \$56.0 million, losses on equity method investment of \$16.4 million and depreciation of \$5.5 million.

Net cash (used in) provided by investing activities

During the nine months ended September 30, 2023, our investing activities used cash of \$77.3 million. The decrease in the nine months ended September 30, 2023 is primarily due to \$754.7 million in marketable securities purchased, offset in part by \$689.9 million of marketable securities maturing, and \$12.5 million in cash for the purchase of property and equipment.

Net cash provided by investing activities in the nine months ended September 30, 2022 is primarily due to \$437.4 million in marketable securities maturing, offset in part by \$192.6 million of marketable securities purchased, \$44.8 million in net cash for the acquisition of Rewrite, and \$9.6 million in cash for the purchase of property and equipment.

Net cash provided by financing activities

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.

Net cash provided by financing activities of \$77.2 million during the nine months ended September 30, 2022 includes \$62.1 million in net proceeds from at-the-market offerings, \$14.0 million in cash received from the exercise of stock options and \$1.1 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, contingent consideration and equity-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, 2022.

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, 2023. 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, 2022.

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, 2023, we had cash equivalents, restricted cash equivalents and marketable securities of \$964.4 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, 2023.

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, 2023.

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, 2023 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.

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, 2022, 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, 2022.

Summary of the Material Risks Associated with Our Business

- CRISPR/Cas9 genome editing technology has limited clinical validation and has not 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.
- 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 and our ongoing 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.
- *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.
- 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.
- 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.
- 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.
- 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.

- 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 an early 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.
- 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.
- 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.
- 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.
- 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 ability to utilize 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.
- We could be unable to avoid, obtain or invalidate patent rights from third parties necessary to develop, manufacture or commercialize our product candidates in one or more jurisdictions.
- 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.
- 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 is not yet 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. Indeed, no genome editing *in vivo* therapy or genome-edited engineered cell therapy has been approved in the United States (“U.S.”), European Union (“EU”) countries or other key jurisdictions. With regards to CRISPR/Cas9-based therapies specifically, we are in the initial phases of clinically testing

our *in vivo* and *ex vivo* product candidates. Accordingly, 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 lead 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.

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 (“CTA”), 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, 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, and, as a result, we cannot predict the time and cost of product candidate development;
- 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 strategies (“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.

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 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 draft guidance document titled “Human Gene Therapy Products Incorporating Human Genome Editing” that the FDA issued in March 2022;
- 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, human clinical trials utilizing either *in vivo* or *ex vivo* CRISPR-based therapeutics, including our clinical trials for NTLA-2001 for transthyretin (“ATTR”) amyloidosis and NTLA-2002 for hereditary angioedema (“HAE”), are still at a clinical stage. 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 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. We expect to submit these data in advance of the planned Phase 3 trial, which will complement the clinical data collected from female patients of child-bearing potential dosed in the ongoing Phase 1/2 study. We cannot guarantee the timing or outcome of these preclinical studies or whether the FDA may require that additional preclinical studies be conducted before commencement of our Phase 3 trial for NTLA-2002. 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 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 (“MEDSAFE”), 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 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 our ongoing Phase 1/2 study of NTLA-2002. 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 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 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.

Competitors in our efforts to provide 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., 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. and Precision Biosciences, Inc.

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., 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, Pharming Group N.V. and Takeda Pharmaceutical Company Limited.

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 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 contract manufacturing organizations ("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 hiring and retaining the experienced scientific, engineering, quality and manufacturing personnel needed to operate or supervise the necessary manufacturing processes, which 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 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 an early 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 or NTLA-2002 for HAE, or for other product candidates, including NTLA-3001 for alpha-1 antitrypsin deficiency ("AATD") and NTLA-6001 for CD30+ lymphomas, being deemed appropriate for clinical development and ultimately approval by a regulatory agency. In addition, we are identifying collaboration opportunities to advance development of NTLA-6001. 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 NTLA-6001, 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 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 please 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, 2022.

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 Personally Identifiable Information, including Protected Health Information ("PHI"), 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 please see the section titled "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, 2022.

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 a company's attention from its 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 and use of data 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:

- in the U.S., 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"), imposes requirements relating to the privacy, security and transmission of PHI on certain covered healthcare providers, health plans, and healthcare clearinghouses, and their respective business associates that perform services for them that involve the use or disclosure of such information. These laws impose civil and criminal monetary penalties, and give state attorneys

general the authority to file civil actions for damages or injunctions, and attorney's fees, in federal courts to enforce the laws;

- the California Consumer Privacy Act ("CCPA") requires covered companies to provide new disclosures to California consumers and afford such consumers new 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 recently amended by the California Privacy Rights Act ("CPRA"), which became effective on January 1, 2023. The CPRA substantially modified the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information, by 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 compliance and we cannot yet fully determine the impact that the CCPA or other privacy laws, regulations and standards may have on our business;
- broad consumer privacy laws have been passed in an additional twelve states. In addition, other states have passed laws regulating specific aspects of privacy. For example, the state of Washington passed a new law that regulates health and medical information that is not subject to HIPAA and a small number of states have enacted laws that specifically focus on biometric information. Furthermore, other U.S. states, such as New York, Massachusetts and Utah have enacted stringent data security laws;
- around the world, many countries have enacted laws that regulate data protection. In the EU and European Economic Area ("EEA") the collection and use of personal data is regulated by the General Data Protection Regulation ("EU GDPR") and the member states' related data protection and privacy laws, and in the U.K. by its Data Protection Act 2018 and the U.K. General Data Protection Regulation ("U.K. GDPR") (such laws collectively being described as "European Data Protection Law"). Because the European Data Protection Law 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. European Data Protection Law imposes strict requirements, including 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. European Data Protection Law 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, European Data Protection Laws include strict requirements on, and prohibit, the transfer of personal data subject to European Data Protection Law to jurisdictions that have not been deemed by competent authorities to offer "adequate" privacy protections ("third countries"), such as the U.S. in certain circumstances, unless a derogation exists or a valid European Data Protection Law transfer mechanism (for example, the European Commission approved Standard Contractual Clauses ("SCCs") and the U.K. International Data Transfer Agreement/Addendum ("U.K. IDTA")) has been put in place and a transfer impact assessment has been carried out. Our compliance with international data transfer obligations under European Data Protection Law, 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 European Commission 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 European Commission. Failure to comply with the requirements of the European Data Protection Law 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 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 European Data Protection Law, may be onerous and adversely affect our business, financial condition, results of operations and prospects. We may also need to rely on multiple third parties 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, 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 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 our results of operations. Any action for 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 please 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, 2022.

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.

Current legislation at the U.S. federal and state levels seeks to reduce healthcare costs and improve the quality of healthcare. For example, the U.S. Affordable Care Act (“ACA”), enacted in March 2010, subjected biologic products to potential competition by lower-cost biosimilars; introduced a new methodology to calculate manufacturers’ rebates under the Medicaid Drug Rebate Program for certain drugs, including infused or injected drugs; increased manufacturers’ minimum Medicaid rebates under the Medicaid Drug Rebate Program; extended the Medicaid Drug Rebate Program to pharmaceutical prescriptions of individuals enrolled in Medicaid managed care organizations; imposed new annual fees and taxes for certain branded prescription drugs and biologic agents; created the Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts as of January 1, 2019, off negotiated prices on certain brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D; and provided incentives to programs that increase the federal government’s comparative effectiveness research. Congress also could consider additional legislation to repeal, replace, or further modify elements of the ACA. Thus, the full impact of the ACA, or any law replacing elements of it, and the political uncertainty regarding any repeal and replacement on the ACA, on our business remains unclear.

In addition, the Inflation Reduction Act of 2022 (“IRA”) includes several provisions that may impact our business to varying degrees, e.g., provisions that effectively eliminate the coverage gap under Medicare Part D, impose new manufacturer financial liability on certain drugs under Medicare Part D, and allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition. Further, President Biden has issued multiple executive orders that have sought to reduce prescription drug costs, and both the Biden administration and Congress

have indicated that they will continue to seek new legislative measures to control drug costs. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA's Medicare drug price negotiation program. The effects of the IRA and these other recent developments on our business and the healthcare industry in general is not yet known.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. As indicated previously, significant uncertainty exists regarding the future scope and effect of current healthcare legislation and regulations because of recent changes in U.S. executive and legislative branches, and elected officials' public declarations of their intention to significantly modify or repeal the current legislative framework. We cannot predict the initiatives that may be adopted in the future, any of which could limit or modify the amounts that foreign, federal and state governments as well as private payors, including patients, will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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, 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 security breaches 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 breaches and failures. Further, having an increasingly 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, 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 and our company or our service providers may be impacted by such attacks in the future. Significant disruptions of these information technology systems or security breaches 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. For example, any such event that leads 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 federal and/or state breach notification laws and foreign law equivalents (such as the U.K. GDPR or the U.K.'s Data Protection Act), and otherwise subject us to liability, including financial penalties and fines, under laws and regulations that protect the privacy and security of personal information. 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. Security breaches, insider threats and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type 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 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. Additionally, artificial intelligence (“AI”) based platforms are increasingly being used in the biopharmaceutical industry. 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 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 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:

- selecting commercially viable product candidates and effective delivery methods;
- successfully completing research, preclinical and clinical development of product candidates;
- obtaining regulatory approvals and marketing authorizations for product;
- 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;
- investing resources in developing commercial manufacturing and operational infrastructure prior to clinical evidence of safety and efficacy for a given product candidate;
- 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;
- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- 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;
- 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; and
- attracting, hiring and retaining qualified personnel.

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 limited 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 the preclinical development or clinical stage. 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 limited 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 \$349.0 million for the nine months ended September 30, 2023. As of September 30, 2023, we had an accumulated deficit of \$1,526.2 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 or other future public health concerns, 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. For example, the FDA's average review times at the agency have fluctuated in recent years as a result of these factors in the U.S. 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.

Disruptions at the FDA and other similar agencies may also slow the time necessary for new product applications to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including beginning on December 22, 2018, 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 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 our condensed consolidated financial statements of this Quarterly Report on Form 10-Q, we have entered into co-development and co-promotion ("Co/Co") 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 Novartis Institutes for BioMedical Research, Inc. ("Novartis") and Regeneron, that we believe can provide such capabilities. 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 Therapeutics, Inc. (“Rewrite”) in order to add additional capabilities to our growing platform. 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 AvenCell

We launched a new company, AvenCell, alongside Cellex Cell Professionals GmbH and Blackstone Life Sciences Advisors L.L.C. We are exposed to risks associated with the launch of the new company and may not realize the advantages we expect from it.

In July 2021, we launched AvenCell alongside Cellex Cell Professionals GmbH (“Cellex”) and Blackstone Life Sciences Advisors L.L.C. (“BXLs”). AvenCell acquired GEMoaB GmbH (“GEMoaB”), a wholly owned subsidiary of Cellex. AvenCell combines GEMoaB’s clinical-stage universal CAR-T program and platforms with our allogeneic universal cell engineering platform, which we licensed to AvenCell pursuant to a license and collaboration agreement with AvenCell (the “AvenCell License”). Under the AvenCell License, we will collaborate with AvenCell to develop at least seven allogeneic universal CAR-T cell therapies. AvenCell may not be successful in the timeframe we expect, or at all. In addition, if AvenCell fails to develop, obtain regulatory approval for or ultimately commercialize any product candidate from its development programs, including those governed by the respective AvenCell License, or breaches or terminates such agreements, our business, financial condition, results of operations and prospects could be harmed.

Additionally, we, BXLs, and Cellex (together with certain related entities) each have equal ownership of AvenCell and, therefore, share control over portions of the operations of AvenCell. Because of our minority ownership in AvenCell, we have a lesser degree of control over its business operations than our own, thereby potentially increasing the financial, legal, operational and compliance risks Intellia may face in the future. In addition, we may be dependent on controlling shareholders or management of AvenCell who may have business interests, strategies or goals that are inconsistent with ours. These risks include the possibility that AvenCell, BXLs or Cellex has economic or business interests or goals that are or become inconsistent with our economic or business interests or goals; is in a position to take action contrary to our instructions, requests, policies or objectives; subjects us to unexpected liabilities or risks; takes actions that reduce our return on investment; acts in a manner that compromises our key licensed rights, or important IP or other rights that we own or license; or takes actions that harm our reputation or restrict our ability to run our business. Furthermore, as a result of our ownership in AvenCell, we are required to include AvenCell’s financial information in our consolidated financial results. This could subject us to increased risk in accurately representing and incorporating AvenCell’s financial statements into our own, which could result in delayed filings with the SEC and the finding of a material or significant weakness, among others. This could result in harmful consequences to our business, including an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements.

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 have only recently begun to manufacture and process product candidate components on a clinical scale and may not be able to successfully complete or continue to do so. We will make changes to optimize the manufacturing process, and cannot be sure that even minor changes in the process will result in therapies that are safe, pure and potent.

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 current good manufacturing practice (“cGMP”), and in certain cases, current good tissue practice (“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 good clinical practice (“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 European Data Protection Law, we could be subject to substantial fines and other penalties, including fines of up to 10,000,000 Euros or up to 2% of our total worldwide annual turnover for certain comparatively minor offenses, or up to 20,000,000 Euros or up to 4% of our total worldwide annual turnover for more serious offenses.

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 Employee Matters and Managing Our Growth

Risks Related to Hiring and Retention

We expect to expand our research, development, manufacturing, clinical and regulatory capabilities, and, as a result, we may encounter difficulties in hiring capable personnel and otherwise managing our growth, which could disrupt our operations.

We expect growth in the number of our employees and the scope of our operations, if any product candidates receive marketing approval, sales, marketing and distribution. To manage our anticipated growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities, and recruit and train additional qualified personnel. Due to

our limited financial resources, the significant competition for employees in our market and industry, and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to recruit and train additional qualified personnel or otherwise effectively manage the expansion of our operations, which may lead to significant costs and divert our management and business resources. Any inability to manage growth could delay or disrupt the execution of our business and operational plans.

****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, 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, Glenn Goddard, 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, 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.

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 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 approved neither any *in vivo* gene editing-based therapeutic nor any nuclease edited cell 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 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 our 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 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 drug 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. 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 for NTLA-2001 for the treatment of ATTR amyloidosis and NTLA-2002 for 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. Depending on what changes the FDA may make to its 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 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 cGMP and GCP, and in certain cases, 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 agency 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. 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, 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, 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 similar foreign regulatory bodies; 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, or Brexit, became effective on January 31, 2020. EU laws, including pharmaceutical laws, continued to apply in the U.K. during a transitional period, which ended on December 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 will continue to apply in Northern Ireland). The regulatory regime in Great Britain therefore currently aligns in 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 new 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 EEA-wide marketing authorizations from the EMA for medicinal products and a separate process for authorization of drug products is required in Great Britain. Until December 31, 2023, the U.K.'s MHRA may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization, however a separate application is required. From January 1, 2024, a new international recognition framework will be put in place in the U.K. (which will be known as the International Recognition Procedure, or 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 any potential collaborators, clinical investigators, CMOs, CROs, consultants or vendors may be 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 HIPAA, as amended by 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 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 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 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 will involve research using research animals and the use of hazardous and flammable materials, including chemicals and biological materials. Our operations 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 401K plans), discrimination, workplace safety and health, benefits, 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". 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 this law. In addition, 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 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 (“mRNA”) 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 of which we are currently unaware 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 infringes these patents. If any such third party patents were held by a court of competent jurisdiction to cover our technologies or product candidates, the holders of any such patents may be able to block our ability to commercialize the applicable product candidate 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, 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 our proposed future product candidates thereby causing us significant harm. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. 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 may be impaired or delayed, which could in turn significantly 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. For example, through 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 (from whom we do not have sublicense rights), we refer to this co-owned worldwide patent portfolio as the “UC/Vienna/Charpentier patent family.” UC/Vienna could challenge Caribou’s rights under their license 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 license agreement with Caribou.

On June 16, 2021, we executed a leaseback agreement with Caribou, which settled the arbitration with Caribou. Under the leaseback agreement, in exchange for an upfront payment, potential future regulatory and sales milestones, and single-digit royalties payable by Caribou to us, we have agreed to leaseback or sublicense certain CRISPR/Cas9 IP, including our chemical gRNA modification technology and foundational CRISPR/Cas9 IP, to Caribou so that it can develop and commercialize CB-010. Caribou also will be responsible for any payments required in respect of our in-licensed IP, such as the foundational CRISPR/Cas9 IP. Under the leaseback agreement, Caribou will be able to compete with us (or our licensees) in the development of CAR-T cell human therapeutics directed at CD19, which could adversely affect our business.

Third parties could assert that UC/Vienna/Charpentier do not have rights to the CRISPR/Cas9 technology, including inventorship and ownership rights to currently issued or allowable patents, or that any rights owned by UC/Vienna/Charpentier are limited. If such third parties were found to have rights to the CRISPR/Cas9 technology, we could be required to obtain rights from such parties or cease our development and commercialization efforts. For example, under our sublicense from Caribou, 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 patents covering the 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.

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 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 their respective interference, 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, 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 the claims of one or more of these parties to 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, these third parties, and others, 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, 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.

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, Novartis and Ospedale San Raffaele ("OSR"). 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.

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, OSR and 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 titled “*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 Confidentiality

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, please 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 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.***

As of June 30, 2023, our executive officers, directors, 5% or greater stockholders and their affiliates beneficially owned approximately 31.5% 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 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, 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 in addition to the proceeds we received from our initial public offering (“IPO”) in May 2016 and follow-on public offerings since then. 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.

In March 2022, we entered into an Open Market Sale Agreement (the “2022 Sale Agreement”) with the Sales Agent, to provide for the offering, issuance and sale of up to an aggregate amount of \$400.0 million of our common stock from time to time in “at-the-market” offerings. We will pay to the Sales Agent cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2022 Sale Agreement. Through September 30, 2023, we issued 3,836,020 shares of our common stock at an average price of \$55.22 per share in accordance with the 2022 Sale Agreement for aggregate net proceeds of \$205.2 million, after payment of cash commissions to the Sales Agent and approximately \$0.3 million related to legal, accounting and other fees in connection with the sales. 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. Persons who were our stockholders prior to our IPO

continue to hold a substantial number of shares of our common stock that many of them are now able to sell in the public market. Significant portions of these shares are held by a relatively small number of stockholders. Sales by our stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock.

Given the volatility in the capital markets, we may not be willing or able to continue to raise equity capital through our ATM program. 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.

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver a placement notice to the Sales Agent at any time throughout the term of the Sale Agreement. The number of shares that are sold by the Sales Agent after delivering a placement notice will fluctuate based on the market price of our common stock during the sales period and limits we set with the Sales Agent in any instruction to sell shares, and the demand for our common stock during the sales period. Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares or the gross proceeds to be raised in connection with those sales, if any, that will be ultimately issued.

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, 2022, we had federal and state NOLs of \$852.1 million and \$797.8 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, 2022, we had federal and state research and development and other credit carryforwards of approximately \$63.4 million and \$48.0 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. This analysis is not expected to result in a material limitation to our other tax attributes. 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

None.

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 dated May 11, 2016. \(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 May 17, 2016\)](#)
- 3.2 [Amendment to the Second Amended and Restated Certificate of Incorporation of the Registrant dated June 14, 2023. \(incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K \(File No. 001-37766\), filed with the Securities and Exchange Commission on June 16, 2023\)](#)
- 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\)](#)
- 10.1† [Letter Agreement \(Second Amendment\) to License and Collaboration Agreement by and between Registrant and Regeneron Pharmaceuticals, Inc., dated November 22, 2022. \(1\)](#)
- 10.2† [Third Amendment to License and Collaboration Agreement by and between Registrant and Regeneron Pharmaceuticals, Inc., dated September 29, 2023. \(1\)](#)
- 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 Glenn Goddard, Executive Vice President, Chief Financial Officer of the Company. \(2\)](#)
- 101.INS Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document. (1)
- 101.SCH Inline XBRL Taxonomy Extension Schema Document. (1)
- 101.CAL Inline XBRL Taxonomy Extension Calculation Linkbase Document. (1)
- 101.DEF Inline XBRL Taxonomy Extension Definition Linkbase Document. (1)
- 101.LAB Inline XBRL Taxonomy Extension Label Linkbase Document. (1)
- 101.PRE Inline XBRL Taxonomy Extension Presentation Linkbase Document. (1)
- 104 Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101) (1)

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10) of Regulation S-K.

(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 9, 2023

INTELLIA THERAPEUTICS, INC.

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

By: /s/ Glenn G. Goddard
Glenn G. Goddard
Executive Vice President, Chief Financial Officer
(Principal Financial and Accounting Officer)

Portions of this Exhibit have been redacted because they are both (i) not material and (ii) would be competitively harmful if publicly disclosed. Information that was omitted has been noted in this document with a placeholder identified by the mark “[***]”.



Kerry K. Reinertsen, Ph.D.
Senior Vice President, Strategic Alliances

Regeneron Pharmaceuticals, Inc.
777 Old Saw Mill River Road
Tarrytown, NY 10591-6707
Phone [***]
Fax [***]
[***]
www.regeneron.com

November 22, 2022

Via FedEx and Electronic Mail

Derek Hicks
Executive Vice President, Chief Business Officer Intellia Therapeutics, Inc.
40 Erie Street
Cambridge, MA 02139
via email at [***]

RE: Use of Regeneron Materials for [***] Intellia Target Evaluation Programs [***]

Dear Mr. Hicks:

Reference is hereby made to the License and Collaboration Agreement dated April 11, 2016, as amended by Amendment 1 dated May 20, 2020 (collectively, as amended, the “**LCA**”) by and between Regeneron Pharmaceuticals Inc. (“**Regeneron**”) and Intellia Therapeutics, Inc. (“**Intellia**”).

Whereas, the Parties wish to amend the LCA through this letter agreement (“**Letter Agreement**”) to enable the Parties to jointly perform additional research activities and for Regeneron to provide access to certain Regeneron Materials and Regeneron Contributed IP for utilization in the advancement of [***] Intellia Liver Targets.

In consideration of the applicable mutual undertakings contained herein and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties, intending to be legally bound, hereby agree as follows:

The Parties mutually filed Patent Applications [***], comprising, *inter alia*, Technology Collaboration Inventions [***]. The Parties have agreed, and hereby agree, to file Patent Applications [***] that relate to or cover Technology Collaboration Inventions, which will be jointly owned by the Parties, and also Patent Applications [***] that solely relate to or cover Regeneration Product Inventions [***], which will be owned by Regeneron. The Parties agree to coordinate regarding the prosecution and maintenance [***] in accordance with Section 10 of the LCA.

The [***] Intellia Liver Targets shall hereby be considered Intellia Evaluation Targets under the LCA. Notwithstanding any contradictory provision of the LCA, including [***], the [***] Intellia Evaluation Targets shall not count against any annual or concurrent limitations or caps related to the Intellia Target Evaluation Programs (e.g., the [***] Intellia Evaluation Targets shall not count against the limitation of selecting [***] Intellia Liver Targets for inclusion in the Intellia Target Evaluation Programs in any given Contract Year or the cap [***] Intellia Target Evaluation Programs at any given time). Unless the Parties agree to extend the Intellia Target Evaluation Program for the [***] Intellia Liver Targets, each of the [***] Intellia Liver Targets shall individually remain an Intellia Evaluation Target until either (a) Intellia presents an Option Package to Regeneron for such Target, or (b) such Target becomes an Intellia Abandoned Target pursuant to Section 5.1(a) (ii) of the LCA.

Notwithstanding any contradictory provision of the LCA, including Sections [***], the [***] Intellia Target Evaluation Programs shall involve Regeneron providing to Intellia [***], and performing certain specific activities related thereto as set forth in the applicable Intellia Target Evaluation Plan. Within [***] days after the date of this Letter Agreement, the JSC shall review and approve the applicable Intellia Target Evaluation Plans for the [***] Intellia Target Evaluation Programs. In accordance with [***] the JSC shall exchange and review scientific information and data from activities being conducted under the [***] Intellia Target Evaluation Plans, and establish processes for the exchange of information relating to such activities. Each Party shall report the progress and results of its activities under the [***] Intellia Target Evaluation Plan to the JSC in accordance with [***] or as otherwise set forth in the applicable Intellia Target Evaluation Plan approved by the JSC. Notwithstanding the foregoing, each Party shall keep the other Party reasonably informed of the progress and results of the [***] Intellia Target Evaluation Programs, including by providing to the other Party a quarterly update and data from experiments and other activities performed by such Party.

Notwithstanding any contradictory provision of the LCA, including [***] and [***], the Parties mutually agree that:

- (1) Regeneron's [***] technology [***] provided to Intellia under the [***] Intellia Target Evaluation Programs shall be considered Regeneron Contributed Technology (and related Know-How or Patents, Regeneron Contributed IP);
 - (2) the definition of Regeneron Contributed Technology (and the related definition of Regeneron Contributed IP) is hereby amended to include technology Controlled by Regeneron or its Affiliates and that Regeneron contributes for its or
-

Intellia's use in the performance of the [***] Intellia Target Evaluation Programs, specifically a new subsection [***] is added to the definition of Regeneron Contributed Technology;

(3) [***] shall be considered Regeneron Materials, and the Agreement is hereby amended to add a definition of [***];

(4) any improvement, enhancement, or other modification that is specific to any Regeneron Materials [***] shall be considered a Regeneron Materials Improvement. [***];

(5) any Intellectual Property that is invented by or on behalf of either Party (or by the Parties jointly) in the performance of activities under the [***] Intellia Target Evaluation Programs, including Joint Improvements and Patent Rights to the extent within any of the foregoing Intellectual Property, other than Regeneron Materials Improvements, Regeneron RGC Inventions, Intellia CRISPR-Cas IP, Intellia Materials Improvements and Intellia Liver Product Inventions (as defined below), shall be considered an Intellia Target Evaluation Program Invention; provided that, notwithstanding the foregoing or any contradictory provision of the LCA, Intellia shall have the right to solely own all [***], which would be considered Intellia Intellectual Property and the terms and conditions of Article 10 of the LCA that are applicable to Intellia Materials Improvements would apply, *mutatis mutandis*, to [***]:

[***].

Regeneron shall provide and transfer to Intellia the foregoing Regeneron Contributed Technology and Regeneron Materials, and any other Regeneron Contributed Technology or Regeneron Materials set forth in the applicable Intellia Target Evaluation Plan. In addition, in accordance with [***], the JSC shall discuss which additional Regeneron Contributed Technology may be useful for the conduct of the [***] Intellia Target Evaluation Programs.

Prior to filing any Patent Application or seeking any Patent Rights related to or arising from the [***], each Party will cooperate with the other Party and the filing Party will provide a copy of any Patent Application to the non-filing Party for review at least [***] days prior to filing such Patent Application. The filing Party shall consider in good faith any of the non-filing Party's comments on such Patent Application. Notwithstanding the foregoing, [***].

In addition to the licenses granted in the LCA, including [***], with respect to the [***] Intellia Evaluation Targets under the applicable Intellia Target Evaluation Programs, Regeneron shall grant, and hereby grants, to Intellia a non-exclusive, worldwide license under Regeneron Materials Improvements and that portion of the Regeneron Contributed IP that is necessary or useful to perform the activities designated to Intellia under the Intellia Target Evaluation Program for [***] during the Option Period. Intellia may sublicense the foregoing license (i) only in accordance with [***] and as necessary to enable permitted subcontractors under, and in accordance with, [***] to perform certain of

Intellia's obligations under the applicable Intellia Target Evaluation Plan and (ii) subject to obtaining Regeneron's prior written consent, which consent will not be unreasonably withheld, conditioned or delayed (which consent may be provided by e-mail), and which consent will be deemed to have already been granted to the extent such subcontracted activity (including the identity of the subcontractor) is specified in the applicable Intellia Target Evaluation Plan.

The Parties hereby agree that any Option Package delivered by Intellia to Regeneron for the [***] Intellia Evaluation Target, as applicable, shall contain [***].

On an Intellia Evaluation Target-by-Intellia Evaluation Target basis, upon selection of a Lead Candidate for the [***] Intellia Liver Target, as applicable, which incorporates or uses Regeneron Contributed Technology ([***]), Regeneron shall grant, and hereby grants, to Intellia a non-exclusive, worldwide license under [***] that is necessary or useful to research, develop, make, have made, use, sell, offer for sale and import Intellia Liver Products Directed to [***], for any and all uses in the Field. [***].

Unless otherwise indicated, all capitalized terms used and not defined in this Letter Agreement shall have the meaning set forth for such terms in the LCA. All section references in this Letter Agreement shall refer to the applicable section of the LCA. Except as explicitly provided in this Letter Agreement, the LCA is not amended by this Letter Agreement. In the event of any conflict between the LCA and this Letter Agreement, this Letter Agreement will control with respect to the subject matter and the terms and conditions contained herein, and otherwise the LCA will control.

This Letter Agreement is specific to the subject matter and the terms and conditions contained herein, and shall not apply to any Intellia Liver Targets other than [***] or other circumstances without the written agreement of the Parties. No provision in this Letter Agreement shall be amended except in a writing executed by an authorized representative of each of the Parties.

This Letter Agreement may be executed in counterparts, each of which shall be deemed an original, but which together shall constitute one and the same instrument and the Parties hereby agree that any electronic or facsimile signatures hereto are legal, valid and enforceable as originals. The language of this Letter Agreement shall be deemed to be the language mutually chosen by the Parties and no rule of strict construction shall be applied against either Party. Intellia and Regeneron have caused this Letter Agreement to be executed by their duly authorized representatives.

Sincerely,

By: /s/ Kerry Reinertsen
Kerry Reinertsen, Ph.D.
Senior Vice President, Strategic Alliances
Regeneron Pharmaceuticals, Inc.

ACKNOWLEDGED AND AGREED:

Intellia Therapeutics, Inc.

By: /s/ Derek Hicks

Name: Derek Hicks

Title: Chief Business Officer

Date: __

cc: [***]

[***]

Exhibit A

[**]

Portions of this Exhibit have been redacted because they are both (i) not material and (ii) would be competitively harmful if publicly disclosed. Information that was omitted has been noted in this document with a placeholder identified by the mark “[***]”.

THIRD AMENDMENT TO LICENSE AND COLLABORATION AGREEMENT

This Third Amendment to the License and Collaboration Agreement (this “Third Amendment”), dated as of September 29, 2023 (the “Third Amendment Date”), is entered into by and between REGENERON PHARMACEUTICALS, INC., a corporation organized under the laws of New York and having a principal place of business at 777 Old Saw Mill River Road, Tarrytown, NY 10591 (“Regeneron”), and INTELLIA THERAPEUTICS, INC., a corporation organized under the laws of Delaware and having a principal place of business at 40 Erie Street, Suite 130, Cambridge, MA 02139 (“Intellia”) (with each of Regeneron and Intellia referred to herein individually as a “Party” and collectively as the “Parties”).

WHEREAS, Regeneron and Intellia entered into that certain License and Collaboration Agreement dated as of April 11, 2016 (the “Original Agreement”), as amended by that certain Amendment 1 to License and Collaboration Agreement dated as of May 30, 2020 (“First Amendment”) and that certain letter agreement dated as of November 22, 2022 (“Second Amendment”) (the Original Agreement, First Amendment and Second Amendment, together, the “Agreement”);

WHEREAS, under the Agreement, Regeneron and Intellia may agree to pursue Non-Liver Targets that are Unavailable Targets;

WHEREAS, Regeneron has developed certain technology to target adeno-associated virus (“AAV”) to non-liver tissues and Intellia has developed certain technology related to [***] Cas proteins derived from *Neisseria meningitidis* for CRISPR-Cas genome editing (“[***]”);

WHEREAS, the Parties desire to collaborate to research and develop candidates for Non-Liver Products that are Directed to certain Non-Liver Targets that are Unavailable Targets as of the Third Amendment Date, which collaboration includes combining Regeneron’s technology for non-liver targeted AAV and Intellia’s technology for [***] NmeCas for CRISPR-Cas genome editing; and

WHEREAS, Regeneron and Intellia desire to amend the Agreement as set forth herein.

NOW, THEREFORE, in consideration of the following mutual promises and obligations, and for other good and valuable consideration the adequacy and sufficiency of which are hereby acknowledged, the Parties agree as follows:

ARTICLE 1 AMENDMENTS

The Parties hereby agree that the Agreement shall be amended as follows:

1.1 Recitals. The recitals of the Agreement are hereby amended by adding the following new recital at the end of the current recitals:

WHEREAS, the Parties have entered into that certain Second Amendment to the License and Collaboration Agreement dated as of November 22, 2022 (the “Second Amendment” and “Second Amendment Date,” respectively), in order to amend this Agreement as set forth therein, which amendment shall be effective as of the Second Amendment Date;

AND WHEREAS, the Parties have entered into that certain Third Amendment to License and Collaboration Agreement dated as of September 29, 2023 (the “Third Amendment” and “Third Amendment Date,” respectively), in order to amend this Agreement as set forth therein, which amendment shall be effective as of the Third Amendment Date.

1.2 Existing Definitions.

(a) Definition of Commercially Reasonable Efforts. The definition of “Commercially Reasonable Efforts” (Section 1.15) in the Agreement is hereby amended by adding “[***]” after the reference to “[***]” in such definition.

(b) Definition of CRISPR-Cas for the Purpose of the EH Collaboration. Article 1 (Definitions) of the Agreement is hereby amended by adding the following paragraph after Section 1.21:

1.21bis “CRISPR-Cas”, [***].

(i) [***].

(c) Definition of Lead Candidate. The definition of “Lead Candidate” (Section 1.66) in the Agreement is hereby amended by adding “or [***]” after the reference to “Intellia Liver Product” in such definition.

(d) Definition of Plans. The definition of “Plans” (Section 1.92) in the Agreement is hereby amended by adding “the EH Collaboration Plans” after the reference to “the Technology Collaboration Plan” in such definition.

(e) Definition of Regeneron Contributed Technology. The definition of “Regeneron Contributed Technology” (Section 1.103) in the Agreement is hereby deleted in its entirety and replaced with the following:

1.103 “Regeneron Contributed Technology” shall mean technology Controlled by Regeneron or its Affiliates and that Regeneron chooses to contribute under this Agreement for its or Intellia’s use in the performance of, as applicable:

(a) the Technology Collaboration (such technology, the “Technology Collaboration Contributed Technology”),

(b) the Regeneron Target Evaluation Program (such technology, the “Regeneron Target Evaluation Program Contributed Technology”),

(c) the Product R&D Program (such technology, the “Product R&D Program Contributed Technology”),

(d) [***], or

(e) the EH Collaboration (such technology, the “Regeneron EH Contributed Technology”), which Regeneron EH Contributed Technology shall include, *inter alia*, Regeneron’s proprietary [***] technology as set forth in Schedule 1.103;

but in each case, excluding, for clarity, Regeneron’s interest in any [***].

(f) Updated Chart of Defined Terms. The chart of defined terms in Section 1.139 of the Agreement is hereby amended to include the following additional defined terms:

Term	Section Reference
<u>Additional EH Collaboration Target</u>	3.7(b)
<u>Agreement</u>	Preamble
[***]	Preamble
[***] <u>NmeCas</u>	Preamble
<u>AAV</u>	Preamble
<u>Budgeted Deferable Binding Year Increased Costs</u>	3.7(g)(iii)(c)
<u>CRISPR-Cas Materials</u>	1.21
<u>Deferred Binding Year Increased Costs</u>	3.7(g)(iii)(c)
<u>Extrahepatic Collaboration or EH Collaboration</u>	3.7(a)(i)
<u>EH Collaboration Inventions</u>	3.7(a)(ii)
<u>EH Collaboration Option Package</u>	3.7(a)(iii)
<u>EH Collaboration Plan</u>	3.7(c)
<u>EH Collaboration Targets</u>	3.7(a)(iv)
<u>EH Collaboration Term</u>	3.7(a)(v)
<u>EH Product Inventions</u>	3.7(a)(vi)
<u>First Amendment</u>	Preamble
<u>Intellia EH Collaboration Improvements</u>	3.7(h)(i)
<u>Initial EH Collaboration Targets</u>	3.7(a)(iv)
<u>Intellia EH Collaboration Co-Co Agreement</u>	3.7(g)(iii)(C)
<u>Intellia EH Collaboration Co-Co Agreement Negotiation Period</u>	3.7(g)(iii)(C)
<u>Intellia EH Collaboration Co-Co Option</u>	3.7(g)(iii)(A)
<u>Intellia EH Collaboration Co-Co Option Notice</u>	3.7(g)(iii)(C)
<u>Intellia EH Collaboration Co-Co Option Period</u>	3.7(g)(iii)(A)
<u>Intellia EH Collaboration Target</u>	3.7(g)(i)(D)
<u>Intellia EH Contributed Know-How</u>	3.7(a)(vii)

<u>Intellia EH Contributed Patent Rights</u>	3.7(a)(viii)
<u>Intellia EH Contributed Technology</u>	3.7(a)(ix)
<u>Intellia EH Products</u>	3.7(g)(i)(D)
<u>Intellia Target Evaluation Program Contributed Technology</u>	1.103(d)
<u>IP Committee</u>	2.5
Lead Candidate Determination	3.7(g)(i)
[***]	3.7(a)(x)
Original Agreement	Preamble
[***]	3.7(a)(xi)
POC Criteria	3.7(a)(xii)
Regeneron Co-Co Option Period End Date	3.7(g)(ii)(D)
Regeneron EH Collaboration Co-Co Agreement	3.7(g)(ii)(C)
Regeneron EH Collaboration Co-Co Agreement Negotiation Period	3.7(g)(ii)
Regeneron EH Collaboration Co-Co Option	3.7(g)(ii)(A)
Regeneron EH Collaboration Co-Co Option Notice	3.7(g)(ii)I
Regeneron EH Collaboration Co-Co Option Period	3.7(g)(ii)(A)
Regeneron EH Collaboration Improvements	3.7(h)(i)
Regeneron EH Collaboration Target	3.7(g)(i)(D)
<u>Regeneron EH Contributed Technology</u>	1.103
<u>Regeneron EH Products</u>	3.7(g)(i)(D)
<u>Regeneron F9/F8 Co-Co Agreements</u>	3.7(g)(ii)(C)
<u>Third Amendment</u>	Preamble
<u>Third Amendment Date</u>	Preamble

1.3Schedule 1.103 – Regeneron EH Contributed Technology. A new Schedule 1.103 is hereby added to the Agreement as set forth on Exhibit 1 attached hereto.

1.4Schedule 3.7(a)(iii) – EH Collaboration Targets. A new Schedule 3.7(a)(iii) is hereby added to the Agreement as set forth on Exhibit 2 attached hereto.

1.5Schedule 3.7(a)(vii) – Intellia EH Contributed Know-How. A new Schedule 3.7(a)(vii) is hereby added to the Agreement as set forth on Exhibit 3 attached hereto.

1.6Schedule 3.7(a)(viii) – Intellia EH Contributed Patent Rights. A new Schedule 3.7(a)(viii) is hereby added to the Agreement as set forth on Exhibit 4 attached hereto.

1.7Schedule 3.7(c)(i) – Initial EH Collaboration Plan. A new Schedule 3.7(c)(i) is hereby added to the Agreement as set forth on Exhibit 5 attached hereto.

1.8Agreement Overview.

(a) Section 2.1(e) of the Agreement is hereby deleted in its entirety and replaced with the following:

(e) the EH Collaboration consisting of EH Collaboration Target-specific research and development activities related to the research and development of Non-Liver Products that are Directed to each such EH Collaboration Target, as more particularly described in Section 3.7, pursuant to which each Party shall perform certain activities as set forth in the applicable EH Collaboration Plan; and

(b) The following provision is hereby added as Section 2.1(f) of the Agreement:

(f) the option for each Party to enter into a [***] cost and profit arrangement for certain Regeneron Products, Intellia CPs, Intellia EH Products, or Regeneron EH Products, as further described herein.

1.9 Joint Steering Committee.

(a) Decision-Making.

(i) Section 2.2(b)(iii)(2) of the Agreement is hereby deleted in its entirety and replaced with the

[***]

(ii) Section 2.2(b)(iii)(3) of the Agreement is hereby deleted in its entirety and replaced with the

[***]

(iii) Section 2.2(b)(iii)(5) of the Agreement is hereby deleted in its entirety and replaced with the

with respect to all other disputes under the scope of the JSC [***], such disputes shall be submitted to the resolution procedures of Section 17.1; and

(b) JSC Duties.

(i) Section 2.2(d)(i) is hereby deleted in its entirety and replaced with the following:

set the overarching research objectives for the Technology Collaboration and EH Collaboration and oversee the general strategies and activities undertaken by the Parties under the Technology Collaboration, EH Collaboration, and the Product R&D Programs;

(ii) Section 2.2(d)(ii) is hereby deleted in its entirety and replaced with the following:

approve the Technology Collaboration Plan (including the annual budget for each Party to be included therein with costs allocated to the Parties, [***]) to conduct the activities under such Technology Collaboration Plan and (B) approve the EH Collaboration Plans (including the annual budget for each Party to be included therein with costs allocated to the Parties, [***]) to conduct the activities under the EH Collaboration Plans;

(iii) Section 2.2(d)(ix) is hereby deleted in its entirety and replaced with the following:

exchange and review scientific information and data from activities being conducted under, and the then-current progress of, the Technology Collaboration Plan, the EH Collaboration Plans, each Regeneron Target Evaluation Plan, each Intellia Target Evaluation Plan, each Product R&D Plan, and Intellia's research and development of Intellia Liver Products [***], and establish processes for the exchange of information relating to such activities;

(iv) The following new Section is inserted as Section 2.2(d)(xv) (and the existing Sections 2.2(d)(xv) and 2.2(d)(xvi) are renumbered as Sections 2.2(d)(xvi) and 2.2(d)(xvii), respectively) and is hereby added to the Agreement as follows:

discuss which Intellia Materials, Intellia Intellectual Property, Intellia EH Contributed Technology, Intellia EH Collaboration Improvements, Regeneron Materials, Regeneron EH Contributed Technology, and Regeneron EH Collaboration Improvements may be useful for the conduct of the EH Collaboration and facilitate the transfer of such materials, information and Know-How to the other Party pursuant to Section 2.2(f);

1.10 Addition of IP Committee. The following new Section 2.5 is hereby added to the Agreement as follows:

2.5 IP Committee. The Parties shall establish a sub-committee of the JSC to provide a collaborative forum for the Parties to discuss intellectual property issues related to the Agreement ("IP Committee"), including [***].

1.11 EH Collaboration Funding.

(a) Section 3.4 is hereby amended by adding "and EH Collaboration" after each occurrence of "Technology Collaboration" and by adding "and EH Collaboration Plan" after each occurrence of "Technology Collaboration Plan."

(b) Section 3.4(a) is further amended by adding the following to the end of the section: "For clarity, for the purposes of this Section 3.4 [***]."

(c) Section 3.4(d) is further amended by adding the following to the end of the section: "For clarity, solely for the purposes of the EH Collaboration, [***]."

1.12 Addition of EH Collaboration. The following new Section 3.7 (EH Collaboration) is hereby added to the Agreement as follows:

3.7 EH Collaboration.

(a) EH Collaboration Definitions.

(i) “Extrahepatic Collaboration” or “EH Collaboration” shall mean the research and development activities to be performed under this Agreement pursuant to the EH Collaboration Plans, for the purpose of developing Non-Liver Products that are Directed to the EH Collaboration Targets.

(ii) “EH Collaboration Inventions” shall mean [***].

(iii) “EH Collaboration Option Package” shall mean, with respect to a Party that has exercised its right to lead a program pursuant to Section 3.7(g), the following information related to all Non-Liver Products Directed to a given EH Collaboration Target that has achieved Lead Candidate Determination to be provided to the other Party pursuant to Section 3.7(g):

(a) [***];

(b) [***];

(c) [***];

(d) [***]; and

(e) such other information as reasonably determined by the JSC.

(iv) “EH Collaboration Targets” shall mean [***].

(v) “EH Collaboration Term” shall mean, on an EH Collaboration Target-by-EH Collaboration Target basis, the period commencing on the date that such EH Collaboration Target is included in the EH Collaboration and expiring on the first to occur of [***].

(vi) “EH Product Inventions” shall mean (a) all Intellectual Property that is invented by or on behalf of either Party (or by the Parties jointly) in the performance of (i) activities under the EH Collaboration or (ii) development, manufacture, or commercialization of any Non-Liver Product that is Directed to an EH Collaboration Target, [***].

(vii) “Intellia EH Contributed Know-How” shall mean, solely for the purposes of the EH Collaboration, any and all Know-How that satisfies [***].

(viii) “Intellia EH Contributed Patent Rights” shall mean, solely for the purposes of the EH Collaboration, those Patent Rights that [***]. The Intellia EH Contributed Patent Rights include those set forth in Schedule 3.7(a)(viii). For the avoidance of doubt, (x) the

use of the defined term “Intellia EH Contributed Patent Rights” shall be for the purpose of [***].

(ix) “Intellia EH Contributed Technology” shall mean, collectively, Intellia EH Contributed Patent Rights and Intellia EH Contributed Know-How.

(x) [***].

(xi) [***].

(xii) “POC Criteria” shall mean the proof-of-concept criteria for identification of a Lead Candidate that is Directed to an EH Collaboration Target.

(b) Addition of EH Collaboration Targets. The Parties may (i) designate additional Non-Liver Targets as “Additional EH Collaboration Targets” (each, an “Additional EH Collaboration Target”) and (ii) replace any existing EH Collaboration Targets with other Non-Liver Targets, in each case ((i)-(ii)), by mutual written agreement. Upon such designation or replacement, the Parties shall amend this Agreement pursuant to Section 17.5 to update Schedule 3.7(a) (iii) and, if applicable, use good faith efforts to negotiate and implement any necessary amendments to any EH Collaboration Plan as a result of such designation or replacement.

(c) EH Collaboration Plan. On an EH Collaboration Target-by-EH Collaboration Target basis, with respect to a given EH Collaboration Target, the Parties shall, at a mutually agreed upon time, jointly prepare and mutually agree upon, through approval by the JSC, a project plan for such EH Collaboration Target for the purpose of identifying a Lead Candidate that is Directed to such EH Collaboration Target (an “EH Collaboration Plan”). Such EH Collaboration Plan shall set forth [***]. The initial EH Collaboration Plans are attached hereto as Schedule 3.7(c)(i) and the Parties will use [***] to update such initial EH Collaboration Plans within [***] days of executing this Third Amendment.

(i) Scope. The Parties generally anticipate that the operational responsibility for activities under each EH Collaboration Plan shall be distributed as follows, with:

(A) Intellia leading (1) the design of the genome editing approach using CRISPR-Cas and (2) the performance of the *in vitro* validation;

(B) Regeneron leading (1) the design of the AAV delivery approach and (2) the performance of AAV packaging; and

(C) a Party, or both Parties jointly, as determined by the JSC, leading *in vivo* validation.

(ii) Amendment of EH Collaboration Plans. After the Parties have mutually agreed upon, through approval by the JSC, an EH Collaboration Plan for an EH Collaboration Target, either Party may propose amendments to such EH Collaboration Plan at any meeting of the JSC; provided, that, at a minimum, no later than [***] days prior to the start of a given Contract Year during the EH Collaboration Term for such EH Collaboration

Target, the Parties shall update such EH Collaboration Plan (excluding the budget thereunder) for the upcoming Contract Year for the JSC's review and approval, and within [***] days after such approval, the Parties shall further update such EH Collaboration Plan with a proposed budget (based on Quarters) for such EH Collaboration Plan for the upcoming Contract Year for the JSC's review and approval; provided, however, that if the JSC does not approve such EH Collaboration Plan or budget for such upcoming Contract Year, then the dispute shall be resolved in accordance with Section 2.2(b)(iii)(5).

(iii) Supply Beyond Research. During the EH Collaboration Term for a given EH Collaboration Target, if it is reasonably likely that a Lead Candidate Determination for such Target will occur within the following [***] month period, the JSC shall in good faith discuss options for the manufacture and supply of the corresponding Non-Liver Product beyond research supply, including GMP manufacturing needed to support an IND for the Non-Liver Product Directed to such EH Collaboration Target.

(d) EH Collaboration Performance.

(i) Efforts. Each Party shall use Commercially Reasonable Efforts to perform its activities under each EH Collaboration Plan within the timelines set forth therein and to achieve the goals and deliverables set forth therein. Each Party shall have day-to-day operational control over those activities delegated to such Party in such EH Collaboration Plan.

(ii) Costs. Subject to Section 3.4, expenses incurred under each EH Collaboration Plan shall be shared equally by the Parties.

(iii) Reporting. Each Party shall report the progress and results of its activities under each EH Collaboration Plan to the JSC in accordance with Section 2.2(f). For clarity, all such reports shall be considered the Confidential Information of both Parties, with each Party being treated as the Receiving Party with respect thereto.

(e) End of EH Collaboration Term for an EH Collaboration Target. From and after the expiration or termination of the EH Collaboration Term for an EH Collaboration Target, (i) no further activities shall be conducted by the Parties under any EH Collaboration Plan for such EH Collaboration Target, (ii) the licenses set forth in Section 3.7(f) shall automatically terminate for such EH Collaboration Target, (iii) no additional amount shall be payable pursuant to Section 3.4 for such EH Collaboration Target, if any, other than amounts which had become due and payable prior to the effective date of such expiration or termination and that remain unpaid as of such date, and (iv) if such EH Collaboration Target was an Unavailable Target as of the Third Amendment Date and a Lead Candidate that is Directed to such EH Collaboration Target was not identified under the applicable EH Collaboration Plan during the applicable EH Collaboration Term (or a Lead Candidate that is Directed to such EH Collaboration Target was identified, but neither Party elected to lead the research, development, and commercialization of Non-Liver Products Directed to such EH Collaboration Target), such EH Collaboration Target shall, thereafter, be considered an Unavailable Target and shall no longer be an EH Collaboration Target.

(f) EH Collaboration License Grants.

(i) Grant by Intellia. Intellia shall grant, and hereby grants, to Regeneron a non-exclusive, worldwide license under Intellia Intellectual Property, Intellia EH Contributed Technology, and Intellia EH Collaboration Improvements solely to perform the activities designated to Regeneron under each EH Collaboration Plan during the EH Collaboration Term for the applicable EH Collaboration Target. Regeneron may sublicense the license granted under this Section 3.7(f)(i) (A) only in accordance with Section 7.2(c)(i) and as necessary to enable permitted subcontractors under, and in accordance with, Section 7.2(b) to perform certain of Regeneron's obligations under such EH Collaboration Plan and (B) subject to obtaining Intellia's prior written consent, which consent shall not be unreasonably withheld, conditioned, or delayed, and which consent shall be deemed to have already been granted to the extent such subcontracted activity (including the identity of the subcontractor) is specified in such EH Collaboration Plan. [***].

(ii) Grant by Regeneron. Regeneron shall grant, and hereby grants, to Intellia a non-exclusive, worldwide license under Regeneron EH Contributed Technology and Regeneron EH Collaboration Improvements solely to perform the activities designated to Intellia under each EH Collaboration Plan during the EH Collaboration Term for the applicable EH Collaboration Target. Intellia may sublicense the license granted under this Section 3.7(f)(ii) (A) only in accordance with Section 7.2(c)(i) and as necessary to enable permitted subcontractors under, and in accordance with, Section 7.2(b) to perform certain of Intellia's obligations under such EH Collaboration Plan and (B) subject to obtaining Regeneron's prior written consent, which consent shall not be unreasonably withheld, conditioned, or delayed, and which consent shall be deemed to have already been granted to the extent such subcontracted activity (including the identity of the subcontractor) is specified in such EH Collaboration Plan. [***].

(iii) Third Party Payments. If (A) Intellia (or any of its Affiliates) would owe any payments (including royalties, milestones, or other amounts) for the use of any Intellia EH Contributed Technology or Intellia EH Collaboration Improvements, or (B) Regeneron (or any of its Affiliates) would owe any payments (including royalties, milestones, or other amounts) for the use of any Regeneron EH Contributed Technology or Regeneron EH Collaboration Improvements, in each case ((A)-(B)), it contributes to, or licenses in connection with, an EH Collaboration Plan, then any and all such payments shall be paid by such Party and shall not be considered Plan Costs.

(g) Development of EH Collaboration Targets and EH Collaboration Co-Co Option.

(i) Allocation of EH Collaboration Targets Between the Parties. On an EH Collaboration Target-by-EH Collaboration Target basis, with respect to each EH Collaboration Target, at such time when the Parties mutually agree, [***] (such event, a "Lead Candidate Determination"), the following provisions shall apply, subject to the remaining provisions of this Section 3.7(g):

(A) Intellia shall have the first right to lead the research, development, and commercialization of Non-Liver Products that are Directed to the first EH Collaboration Target that is the subject of a Lead Candidate Determination;

(B) Regeneron shall have the first right to lead the research, development, and commercialization of Non-Liver Products that are Directed to the second EH Collaboration Target that is the subject of a Lead Candidate Determination, and

(C) [***].

(D) If the Party having first right to lead the research, development, and commercialization of a given Non-Liver Product elects not to lead such Product, the other Party shall have the right to do so (and the Party having declined the first right to lead such program shall not have the Option to enter into a Co-Co Agreement in such scenario). Further, if the other Party, who did not have first right to lead such program, elects to lead the research, development, and commercialization of such Non-Liver Product, such Party shall be entitled to advance such Non-Liver Product as per below, and shall not lose its first right to lead the subsequent Non-Liver Product. Following Lead Candidate Determination, each EH Collaboration Target for which Intellia will lead the research, development, and commercialization of Non-Liver Products that are Directed to such EH Collaboration Target will be considered an “Intellia EH Collaboration Target” and such Non-Liver Products will be considered “Intellia EH Products,” and each EH Collaboration Target for which Regeneron will lead the research, development, and commercialization of Non-Liver Products that are Directed to such EH Collaboration Target shall be considered a “Regeneron EH Collaboration Target” and such Non-Liver Products shall be considered “Regeneron EH Products.” Unless otherwise agreed by the Parties, if neither Party elects to lead a given Non-Liver Product within [***] days of Lead Candidate Determination, then the license grants for such Non-Liver Product shall expire in accordance with Section 3.7(g)(v), as if no Lead Candidate Determination had occurred for such EH Collaboration Target. Each Regeneron EH Collaboration Target shall be considered a Regeneron Target independent of and without regards to the Target Selection Period and any such Regeneron EH Collaboration Target will not count against the Regeneron Target Cap, but such Target shall count as one (1) of the [***] Non-Liver Targets permitted to be Regeneron Targets under this Agreement.

(ii) Regeneron EH Collaboration Co-Co Option.

(A) On an Intellia EH Collaboration Target-by-Intellia EH Collaboration Target basis, with respect to a given Intellia EH Collaboration Target, during the period of time commencing on the date (1) a Lead Candidate Determination is made with respect to such EH Collaboration Target and (2) Intellia has elected and notified Regeneron of its desire to lead the research, development, and commercialization of such Non-Liver Product, with such election and notification, as well as furnishing of an EH Collaboration Option Package to Regeneron (if Intellia does elect to lead such program), occurring within [***] days after Lead Candidate Determination, and ending [***] days following Regeneron’s receipt of such EH Collaboration Option Package (the “Regeneron EH Collaboration Co-Co Option Period”), Intellia hereby grants to Regeneron an exclusive

option to enter into a Co-Co Agreement (based on the Form of Co-Co Agreement agreed by the Parties on July 20, 2018) with Intellia for each Intellia EH Collaboration Target and Intellia shall be the Lead Party, as such term is used in the Form of Co-Co Agreement agreed by the Parties on July 20, 2018, with respect thereto (a “Regeneron EH Collaboration Co-Co Option”).

(B) During the Regeneron EH Collaboration Co-Co Option Period, (1) Intellia shall make its personnel reasonably available to answer questions related to the information in the EH Collaboration Option Package, and (2) Intellia shall promptly update Regeneron regarding, and provide to Regeneron, any new data or information that would have otherwise been provided in the EH Collaboration Option Package provided under this Section 3.7(g)(ii).

(C) If Regeneron wishes to exercise a Regeneron EH Collaboration Co-Co Option for a particular Intellia EH Collaboration Target, Regeneron shall provide written notice thereof (the “Regeneron EH Collaboration Co-Co Option Notice”) to Intellia within the Regeneron EH Collaboration Co-Co Option Period. Upon Regeneron’s timely exercise of such Regeneron EH Collaboration Co-Co Option, the Parties shall use good faith efforts to execute a Co-Co Agreement for such Intellia EH Collaboration Target (a “Regeneron EH Collaboration Co-Co Agreement”) within [***] days thereafter (which period may be extended by mutual agreement of the Parties) (the “Regeneron EH Collaboration Co-Co Agreement Negotiation Period”) based on the Form of Co-Co Agreement agreed by the Parties on July 20, 2018, with the specific provisions to be used based on Intellia being the Lead Party, as such term is used in the Form of Co-Co Agreement agreed by the Parties on July 20, 2018 and such additional modifications to the Form of Co-Co Agreement as may be necessary to reflect changes to the Net Sales definition (as reflected in the 2020 Co-Co Agreements for Factor IX and Factor VIII programs lead by Regeneron (“Regeneron F9/F8 Co-Co Agreements”)) and the specific nature of the EH Collaboration, including [***]. No milestone payment or option payment shall be due or payable with respect to Regeneron’s exercise of a Regeneron EH Collaboration Co-Co Option for an Intellia EH Product Directed to such Intellia EH Collaboration Target. The Regeneron EH Collaboration Co-Co Agreement shall not count against the limits on Regeneron Options under Section 5.1(c), and nothing in this Agreement outside of this Section 3.7(g) shall limit the number of Regeneron EH Collaboration Co-Co Options that Regeneron may exercise pursuant to this Section 3.7(g), though such EH Collaboration Target (under the applicable Regeneron EH Collaboration Co-Co Agreement) shall count as one (1) of the [***] Non-Liver Targets permitted to be Regeneron Targets under this Agreement.

(D) If [***], in each case ((1)-(2)) (the “Regeneron Co-Co Option Period End Date”), Intellia shall have the right, but not the obligation, to research, develop, and commercialize the applicable Intellia EH Product pursuant to Section 3.7(g)(ii)(E).

(E) If [***]; provided that:

(1) the license grant will provide that Intellia will have the right to grant sublicenses through multiple tiers (in accordance with Section 7.2(c),

provided further that Intellia shall only have the right to sublicense to Third Parties for those Intellia EH Products that are Intellia CPs), under the Regeneron EH Contributed Technology and Regeneron EH Collaboration Improvements to research, develop, make, have made, use, sell, offer for sale, import and commercially exploit the applicable Intellia EH Products Directed to the applicable Intellia EH Collaboration Target in the Field in the Territory;

(2) in connection with such license, upon the Regeneron Co-Co Option Period End Date, Regeneron will transfer to Intellia any Regeneron Materials and Regeneron Material Improvements included in the Regeneron EH Contributed Technology and Regeneron EH Collaboration Improvements in accordance with Section 7.7 of this Agreement;

(3) except as expressly provided in this Section 3.7(g)(ii)(E), Regeneron shall not be required to grant to Intellia any right, title or interest in or to any other intellectual property rights, materials or Confidential Information of Regeneron or any of its Affiliates (either expressly or by implication or estoppel) with respect to the Intellia EH Products;

(4) under this Section 3.7(g)(ii)(E), Intellia will pay to Regeneron royalties for Intellia EH Products at the rates set forth in the table below based on the stage of the most advanced Non-Liver Product Directed to the applicable EH Collaboration Target as of the effective date that such Non-Liver Product became an Intellia EH Product:

Preclinical Stage of Development	Royalty Rate	
[***]	[***]	
Stage of Clinical Development	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]

(5) The Royalty payments under Section 3.7(g)(ii)(E) shall be subject to and in accordance with the terms and conditions of Sections 9.3(b), 9.4(a), 9.5 (excluding the first proviso in the first sentence that begins “provided that, in no event shall such aggregation...”), 9.6, 9.7, 9.8, 9.9, 9.10, 9.11 and 9.12 and Article 11 and the defined term “Net Sales”, applied *mutatis mutandis* with references to (A) “Regeneron” being deemed to be references to “Intellia,” (B) “Intellia” being deemed to be references to “Regeneron,” (C) “Regeneron Product” being deemed to be references to “Intellia EH Collaboration Products” (only as applicable to Sections 9.3(b), 9.4(a), 9.5 (excluding the first proviso in the first sentence that begins “provided that, in no event shall such aggregation...”), 9.6, 9.7, 9.8, 9.9, 9.10, 9.11 and 9.12 and Article 11 and the defined term “Net Sales”), (D) “Intellia Background Patent Rights” being deemed to be references to “Patent Rights within the Regeneron EH Collaboration Technology,” and (E) and other

defined terms used in such Sections being appropriately modified consistent with the foregoing; and

(6) In addition to the royalties due under Section 3.7(g)(ii)(E), Intellia will be responsible for any and all payments due to a Third Party with respect to any Regeneron EH Contributed Technology that is licensed by Regeneron or any of its Affiliates, and which Intellia has elected to receive a sublicense to pursuant to this Section 3.7(g)(ii)(E)(6), which amounts shall be paid by Intellia within [***] days after receipt of an invoice therefor from Regeneron (“In-Licensed Regeneron EH Contributed IP”). Regeneron shall provide prompt written notice of such In-Licensed Regeneron EH Contributed IP to Intellia, including a redacted copy of each such Third Party agreement therefor (which may be redacted for information not pertinent to this Agreement to the extent that such redactions do not reasonably impair Intellia’s ability to evaluate whether it wants a sublicense under such In-Licensed Regeneron EH Contributed IP), so Intellia may elect whether to include such license under this Section 3.7(g)(ii)(E)(6). If Intellia provides notice that it does elect to include such In-Licensed Regeneron EH Contributed IP within [***] days of receipt of such written notice from Regeneron (together with the redacted copy thereof), then the respective In-Licensed Regeneron EH Contributed IP will be included in the license agreement to be entered into pursuant to this Section 3.7(g)(ii)(E). Any In-Licensed Regeneron EH Contributed IP not selected by Intellia hereunder within such [***] day period, shall not be included in the license agreement to be entered into pursuant to this Section 3.7(g)(ii)(E). Furthermore, notwithstanding anything to the contrary herein, Intellia’s rights under each license with respect to such In-Licensed Regeneron EH Contributed IP elected by Intellia to be included in the license agreement under this Section 3.7(g)(ii)(E) will be subject to the applicable terms and conditions of the applicable Third Party agreement (to the extent such applicable terms and conditions have been disclosed to Intellia hereunder) and Intellia shall comply with, and shall ensure compliance with, the terms and conditions of all such Third Party agreements. In addition, Intellia shall promptly (and in all cases, within the time periods necessary for Regeneron (and its Affiliates, as applicable) to report and otherwise comply with the provisions of its (and its Affiliates’) Third Party agreements) provide to Regeneron all information necessary for Regeneron (and its Affiliates, as applicable) to report and otherwise comply with the provisions of such Third Party agreements, including for purposes of making any payments thereunder.

(F) AAV Manufacturing and Technology Transfer for Intellia EH Products. [***].

(iii) Intellia EH Collaboration Co-Co Option.

(A) On a Regeneron EH Collaboration Target-by-Regeneron EH Collaboration Target basis, with respect to a given Regeneron EH Collaboration Target, during the period of time commencing on the date (1) a Lead Candidate Determination is made with respect to such EH Collaboration Target and (2) Regeneron has elected and

notified Intellia of its desire to lead the research, development, and commercialization of such Non-Liver Product, with such election and notification, as well as furnishing of an EH Collaboration Option Package to Intellia (if Regeneron does elect to lead such program), occurring within [***] days after Lead Candidate Determination, and ending [***] days following Intellia's receipt of such EH Collaboration Option Package (the "Intellia EH Collaboration Co-Co Option Period"), Regeneron hereby grants to Intellia an exclusive option to enter into a Co-Co Agreement (based on the Form of Co-Co Agreement agreed by the Parties on July 20, 2018) with Regeneron for each Regeneron EH Collaboration Target and Regeneron shall be the Lead Party, as such term is used in the Form of Co-Co Agreement agreed by the Parties on July 20, 2018, with respect thereto (a "Intellia EH Collaboration Co-Co Option").

(B) During the Intellia EH Collaboration Co-Co Option Period, (1) Regeneron shall make its personnel reasonably available to answer questions related to the information in the EH Collaboration Option Package, and (2) Regeneron shall promptly update Intellia regarding, and provide to Intellia, any new data or information that would have otherwise been provided in the EH Collaboration Option Package provided under this Section 3.7(g)(iii).

(C) If Intellia wishes to exercise an Intellia EH Collaboration Co-Co Option for a particular Regeneron EH Collaboration Target, Intellia shall provide written notice thereof (the "Intellia EH Collaboration Co-Co Option Notice") to Regeneron within the Intellia EH Collaboration Co-Co Option Period. Upon Intellia's timely exercise of such Intellia EH Collaboration Co-Co Option, the Parties shall use good faith efforts to execute a Co-Co Agreement for such Regeneron EH Collaboration Target (an "Intellia EH Collaboration Co-Co Agreement") within [***] days thereafter (which period may be extended by mutual agreement of the Parties) (the "Intellia EH Collaboration Co-Co Agreement Negotiation Period") based on the Form of Co-Co Agreement agreed by the Parties on July 20, 2018, with the specific provisions to be used based on Regeneron being the Lead Party, as such term is used in the Form of Co-Co Agreement agreed by the Parties on July 20, 2018 [***] and the specific nature of the EH Collaboration, including (1) the definition of [***], (2) the incorporation of Regeneron EH Contributed Technology and any Regeneron EH Collaboration Improvements and (3) that if the Intellia EH Collaboration Co-Co Agreement is terminated and Intellia continues development and commercialization without Regeneron, Intellia shall pay Regeneron financials in accordance with Section 3.7(g)(ii)(E)(4)-(5); provided, however, that in the event that the Parties are unable to mutually agree upon certain provisions of the Intellia EH Collaboration Co-Co Agreement, such dispute shall be submitted to the dispute resolution procedures of Section 17.1. No milestone payment or option payment shall be due or payable with respect to Intellia's exercise of an Intellia EH Collaboration Co-Co Option for a Regeneron EH Product Directed to such Regeneron EH Collaboration Target. The Intellia EH Collaboration Co-Co Agreement shall not count against the limits on Intellia Options under Section 5.2(a), and nothing in this Agreement outside of this Section 3.7(g) shall limit the number of Intellia EH Collaboration Co-Co Options that Intellia may exercise pursuant to this Section 3.7(g).

(D) If Intellia (1) does not exercise an Intellia EH Collaboration Co-Co Option for a particular Regeneron EH Collaboration Target during the applicable Intellia EH Collaboration Co-Co Option Period, or (2) notifies Regeneron in writing that it does not wish to exercise an Intellia EH Collaboration Co-Co Option for a particular Regeneron EH Collaboration Target prior to the end of the Intellia EH Collaboration Co-Co Option Period, in each case ((1)-(2)), Regeneron shall have the right to take such Regeneron EH Product forward as a Regeneron Product that is Directed to a Regeneron Target under the terms and conditions of the Agreement; provided, however, that:

(x) the definition of CRISPR-Cas [***] shall apply with respect to such Regeneron EH Product even when considered a Regeneron Product;

(y) if the Agreement is terminated with respect to such Regeneron EH Product and it becomes a Reversion Product that Intellia thereafter takes forward, Intellia shall pay Regeneron financials in accordance with Section 3.7(g)(ii)(E)(4)-(5) and not Section 16.7(c)(iv); and

(z) each Regeneron EH Collaboration Target shall count as one (1) of the [***] Non-Liver Targets permitted to be Regeneron Targets under this Agreement.

(E) [***].

(iv) Modification of this Agreement by an EH Collaboration Co-Co Agreement. For clarity, in the event that the Parties enter into an Intellia EH Collaboration Co-Co Agreement or Regeneron EH Collaboration Co-Co Agreement, as applicable, such Co-Co Agreement may supersede certain provisions of this Agreement solely with respect to the particular EH Collaboration Target that is the subject of such Co-Co Agreement, which superseded provisions will be expressly identified in such Co-Co Agreement.

(v) No Lead Candidates. If at the end of the EH Collaboration Term for an EH Collaboration Target no Lead Candidates have been identified, this Third Amendment shall terminate with respect to such EH Collaboration Target and all licenses to EH Collaboration Contributed Technology shall expire solely with respect to such EH Collaboration Target.

(h) EH Collaboration IP.

(i) [***].

(ii) [***].

(i) [***].

1.13 Subcontracts and Sublicenses. Section 7.2(b) is hereby amended by adding “[***].” For the avoidance of doubt, if a license is sublicensable under this Third Amendment, the provisions of Section 7.2(c) shall apply to such sublicense.

1.14 Intellia Third Party Agreements. Section 7.3(d) is hereby amended by adding [***].

1.15 Records. Section 7.5 is hereby amended by adding “and EH Collaboration” after “Technology Collaboration” and by adding “and EH Collaboration Plan, as applicable,” after “Technology Collaboration Plan”, in each instance.

1.16 Debarment. Section 7.8 is hereby amended by adding “, EH Collaboration,” after “Technology Collaboration.”

1.17 No Use of Non-Controlled IP in EH Collaboration. Section 7.9 is hereby amended by adding “, EH Collaboration,” after the first “Technology Collaboration” and by adding “or EH Collaboration, as applicable” after the second “Technology Collaboration.”

1.18 Confidentiality. A new sentence is hereby added as the penultimate sentence of Section 13.1(d) of the Agreement as follows:

EH Collaboration Inventions and EH Product Inventions to the extent jointly owned by the Parties shall be Confidential Information of both Parties; provided that the EH Product Inventions may be utilized as provided in Section 13.1(c), as well as, the following: (i) used by either Party (or their respective subcontractors, licensees or sublicensees) but not disclosed to Third Parties except as other Confidential Information may be disclosed by the Receiving Party (a) as expressly permitted herein (including through the publication procedures set forth in Section 13.4) or (b) with the prior written consent of the other Party; (ii) disclosed under commercially reasonable confidentiality terms and solely to the extent reasonably necessary to any potential or actual investor, advisor, lender, investment banker, financing partner, or acquirer; and (iii) disclosed under confidentiality obligations at least as restrictive as, or substantially the same as, those set forth herein [***], to any actual or prospective subcontractor, licensee or sublicensee. Notwithstanding the foregoing or anything to the contrary contained herein, Regeneron EH Collaboration Improvements shall be the Confidential Information of Regeneron, and Intellia EH Collaboration Improvements shall be the Confidential Information of Intellia.

1.19 Disclosures Concerning Agreement; Agreement Terms. Section 13.5(b) is hereby amended by [***].

1.20 Survival of Obligations. A new sentence is hereby added as the penultimate sentence of Section 16.10 of the Agreement as follows:

Further, the provisions of Sections 3.7(h)(i) and 3.7(h)(ii) shall survive the expiration or termination of this Agreement.

ARTICLE 2 REPRESENTATIONS AND WARRANTIES

2.1 Each Party hereto represents and warrants to the other Party, as of the Third Amendment Date, as follows: (a) it is duly organized, validly existing, and in good standing under the laws of its jurisdiction of incorporation; (b) it has full corporate power and authority to execute,

deliver, and perform this Third Amendment, and has taken all corporate action necessary to enter into, deliver, and perform this Third Amendment (including the amendments to the Agreement as set forth herein); (c) the execution and performance by it of its obligations hereunder (including the amendments to the Agreement as set forth herein) shall not constitute a breach of, or conflict with, its organizational documents nor any other material amendment or arrangement, whether written or oral, by which it is bound or requirement of Applicable Laws; (d) this Third Amendment (including the amendments to the Agreement as set forth herein) is its legal, valid, and binding obligation, enforceable in accordance with the terms and conditions hereof (subject to Applicable Laws of bankruptcy and moratorium); (e) such Party is not prohibited by the terms of any agreement to which it is a party from granting the rights or licenses hereunder (including as set forth in the amendments to the Agreement as set forth herein); (f) no broker, finder, or investment banker is entitled to any brokerage, finder's, or other fee in connection with this Third Amendment or the transactions contemplated hereby based on arrangements made by it or on its behalf; and (g) it has obtained all necessary consents, approvals, and authorizations of all Governmental Authorities and other Persons required to be obtained by it as of the Third Amendment Date, as applicable, in connection with the execution, delivery, and performance of this Third Amendment (including the amendments to the Agreement as set forth herein).

ARTICLE 3 EFFECTIVE DATE OF AMENDMENTS TO AGREEMENT

3.1 The amendments to the Agreement as set forth in ARTICLE 1 shall be effective as of the Third Amendment Date.

ARTICLE 4 MISCELLANEOUS

4.1 The Parties may mutually agree to issue a press release announcing the execution of this Third Amendment, and, if the Parties so mutually agree, such press release [***]. Excluding the first sentence, the provisions of Section 13.5(a) of the Agreement are hereby incorporated by reference into this Third Amendment, *mutatis mutandis*.

4.2 The provisions of Section 13.5(d) of the Agreement are hereby incorporated by reference into this Amendment, *mutatis mutandis*; provided that the Parties shall use good faith efforts to agree to a redacted copy of this Third Amendment for filing with the SEC promptly after the Third Amendment Date.

4.3 Capitalized terms used and not defined herein shall have the meanings ascribed to such terms in the Agreement. All references herein to paragraph or section location shall relate to the corresponding paragraph or section in the Agreement.

4.4 Except as specifically set forth in this Third Amendment, the Agreement shall continue in full force and effect without change. If there is any conflict between the terms of this Third Amendment and the Agreement, the terms of this Third Amendment shall govern.

4.5 This Third Amendment may be executed in counterparts, each of which shall be deemed an original, but which together shall constitute one and the same instrument. In addition,

this Third Amendment may be executed by facsimile or “PDF” and such facsimile or “PDF” signature shall be deemed to be an original.

4.6 This Amendment shall be governed by and construed in accordance with the laws of the State of New York, without regard to the conflict of laws principles thereof that would require the application of the law of any other jurisdiction.

4.7 The provisions of Article 17 of the Agreement are hereby incorporated by reference into this Third Amendment, *mutatis mutandis*.

[Signature Page Follows]

IN WITNESS WHEREOF, the Parties have executed this Third Amendment as of the Third Amendment Date.

REGENERON PHARMACEUTICALS, INC.

By: /s/ Nouhad Hussein

Name: Nouhad Hussein

Title: SVP Business Development

INTELLIA THERAPEUTICS, INC.

By: /s/ Derek Hicks

Name: Derek Hicks

Title: Chief Business Officer

[Signature Page to Third Amendment to License and Collaboration Agreement]

Exhibit 1
Schedule 1.103

[***]

Exhibit 2

Schedule 3.7(a)(iii)

[***]

Exhibit 3

Schedule 3.7(a)(vii)

[***]

Exhibit 4

Schedule 3.7(a)(viii)

[***]

Exhibit 5

Schedule 3.7(c)(i)

[***]

**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 9, 2023

/s/ John M. Leonard

John M. Leonard, M.D.

President and Chief Executive Officer

(Principal Executive Officer)

**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, Glenn Goddard, 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 9, 2023

/s/ Glenn Goddard

Glenn Goddard

Executive Vice President, Chief Financial Officer

(Principal Financial and Accounting Officer)

**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, 2023, 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 Glenn Goddard, Executive Vice President and Chief Financial Officer (Principal Financial and Accounting 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 9, 2023

/s/ John M. Leonard

John M. Leonard, M.D.

President and Chief Executive Officer

(Principal Executive Officer)

/s/ Glenn Goddard

Glenn Goddard

Executive Vice President and Chief Financial Officer

(Principal Financial and Accounting Officer)
