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, 2021

OR

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

For the transition period from _____ to

Commission File Number: 001-37766

INTELLIA THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in its Charter)

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

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

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

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

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

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

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

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

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

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

The number of shares outstanding of the registrant's common stock as of October 29, 2021: 74,419,414 shares.

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, 2021	December 31, 2020
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 334,736	$ 160,020
Marketable securities	463,531	437,351
Accounts receivable ($0.2 million and $0 million from related party)	2,491	2,130
Prepaid expenses and other current assets	14,016	17,016
Total current assets	814,774	616,517
Marketable securities - noncurrent	350,451	-
Property and equipment, net	19,946	15,943
Operating lease right-of-use assets	81,788	39,114
Equity method investment	62,837	-
Other assets	5,165	4,748
Total Assets	$ 1,334,961	$ 676,322
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$ 7,470	$ 10,460
Accrued expenses	24,633	25,554
Current portion of operating lease liability	8,705	5,696
Current portion of deferred revenue ($34.2 million and $0 million from related party)	56,759	22,544
Total current liabilities	97,567	64,254
Deferred revenue, net of current portion ($28.5 million and $0 million from related party)	63,023	51,387
Long-term operating lease liability	67,273	33,609
Commitments and contingencies (Note 6)		
Stockholders' Equity:		
Common stock, $0.0001 par value; 120,000,000 shares authorized; 74,342,178 and 66,234,056 shares issued and outstanding at September 30, 2021 and December 31, 2020, respectively	7	7
Additional paid-in capital	1,729,029	962,173
Accumulated other comprehensive (loss)/income	(174)	1
Accumulated deficit	(621,764)	(435,109)
Total stockholders' equity	1,107,098	527,072
Total Liabilities and Stockholders' Equity	$ 1,334,961	$ 676,322

See notes to condensed consolidated financial statements.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Collaboration revenue (1)	$ 7,204	$ 22,220	$ 20,199	$ 51,399
Operating expenses:				
Research and development	60,486	39,756	158,646	112,177
General and administrative	18,711	10,566	48,988	33,406
Total operating expenses	79,197	50,322	207,634	145,583
Operating loss	(71,993)	(28,102)	(187,435)	(94,184)
Interest income	349	262	780	2,145
Net loss	$ (71,644)	$ (27,840)	$ (186,655)	$ (92,039)
Net loss per share, basic and diluted	$ (0.97)	$ (0.47)	$ (2.68)	$ (1.70)
Weighted average shares outstanding, basic and diluted	73,706	58,754	69,720	54,218
Other comprehensive loss:				
Unrealized loss on marketable securities	(161)	(124)	(175)	(230)
Comprehensive loss	$ (71,805)	$ (27,964)	$ (186,830)	$ (92,269)
(1) Including the following revenue from related party (see Notes 7 and 8):	$ 277	$ -	$ 277	$ -

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,	
	2021	**2020**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (186,655)	$ (92,039)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	5,011	4,709
Equity-based compensation	32,448	14,321
Amortization/(accretion) of investment premiums/(discounts)	4,970	(195)
Changes in operating assets and liabilities:		
Accounts receivable	(361)	3,403
Prepaid expenses and other current assets	(5,073)	(1,951)
Operating right-of-use assets	6,761	4,866
Other assets	(248)	348
Accounts payable	(1,870)	3,445
Accrued expenses	(1,170)	6,719
Deferred revenue	(16,986)	50,804
Operating lease liabilities	(7,206)	(4,116)
Net cash used in operating activities	(170,379)	(9,686)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	(9,888)	(2,579)
Purchases of marketable securities	(772,759)	(244,790)
Maturities of marketable securities	390,984	243,800
Net cash used in investing activities	(391,663)	(3,569)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of common stock through follow-on offerings, net of issuance costs	648,315	107,732
Proceeds from issuance of common stock through at-the-market offerings, net of issuance costs	45,255	14,722
Proceeds from issuance of common stock to Regeneron	-	12,580
Proceeds from options exercised	39,868	1,967
Issuance of shares through employee stock purchase plan	970	685
Net cash provided by financing activities	734,408	137,686
Net increase in cash and cash equivalents and restricted cash and cash equivalents	172,366	124,431
Cash and cash equivalents and restricted cash and cash equivalents, beginning of period	164,606	57,226
Cash and cash equivalents and restricted cash and cash equivalents, end of period	$ 336,972	$ 181,657
Reconciliation of cash and cash equivalents and restricted cash and cash equivalents to condensed consolidated balance sheet:		
Cash and cash equivalents	$ 334,736	$ 179,746
Restricted cash and cash equivalents, included in prepaids and other current assets and other assets	2,236	1,911
Total cash and cash equivalents and restricted cash and cash equivalents	$ 336,972	$ 181,657
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Purchases of property and equipment unpaid at period end	$ 633	$ 545
Right-of-use assets acquired under operating leases	49,435	7,939
Non-cash contribution of intellectual property to NewCo	62,900	-

See notes to condensed consolidated financial statements.

1. Overview and Basis of Presentation

Intellia Therapeutics, Inc. ("Intellia" or the "Company") is a leading clinical-stage genome editing company, focused on developing novel, potentially curative therapeutics using CRISPR/Cas9 technology. 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, the Company is pursuing two primary approaches. The Company's *in vivo* programs use intravenously administered CRISPR as the therapy, in which its proprietary delivery technology enables highly precise editing of disease-causing genes directly within specific target tissues. The Company's *ex vivo* programs use CRISPR to create the therapy by using engineered human cells to treat cancer and autoimmune diseases. The Company's deep scientific, technical and clinical development experience, along with its robust intellectual property ("IP") portfolio, enables the Company to unlock broad therapeutic applications of CRISPR/Cas9 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, 2020.

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

During the third quarter of 2021, the Company entered into a joint venture with Cellex Cell Professionals GmbH ("Cellex") and funds managed by Blackstone Life Sciences Advisors L.L.C. ("BXLS") to establish a new chimeric antigen receptor ("CAR-T") cell therapy company ("NewCo"). The Company had a 33.33% investment share in NewCo at the time of the initial closing and accounts for the investment under the equity method of accounting. Refer to Notes 2 and 8 for further details.

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, equity-based compensation expense and the valuation of our equity method investment. 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 extent of the impact of the coronavirus disease 19 ("COVID-19") pandemic on the Company's operational and financial performance will depend on certain developments, including the length and severity of this pandemic, as well as its effect on the Company's employees, collaborators and vendors, all of which are uncertain and cannot be predicted. The Company cannot reasonably estimate the extent to which the disruption may materially impact its consolidated results of operations or financial position.

The effects of material revisions in estimates are 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, 2021, the Company has raised an aggregate of approximately $1,815.7 million to fund its operations, of which $276.8 million was through its collaboration agreements, $170.5 million was from its initial public offering ("IPO") and concurrent private placements, $1,086.9 million was from follow-on public offerings, $196.5 million was from at-the-market offerings and $85.0 million was from the sale of convertible preferred stock. In July 2021, the Company closed an underwritten public offering of 4,758,620 shares of common stock at the public offering price of $145.00 per share, for aggregate net proceeds of $648.3 million after deducting approximately $41.7 million in underwriting discounts and offering costs. The Company expects that its cash, cash equivalents and marketable securities as of September 30, 2021 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, 2020. There have been no material changes during the nine months ended September 30, 2021, other than as noted below.

Variable Interest Entity

The Company evaluates at the inception of each arrangement, and whenever a reconsideration event occurs, whether an entity in which the Company holds an investment or in which the Company has other variable interests is considered a variable interest entity ("VIE") in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") *Topic 810, Consolidation* ("ASC 810"). If the entity meets the criteria to qualify as a VIE, the Company assesses whether or not the Company is the primary beneficiary of that VIE based on a number of factors, including (i) which party has the power to direct the activities that most significantly affect the VIE's economic performance, (ii) the parties' contractual rights and responsibilities pursuant to any contractual agreements and (iii) which party has the obligation to absorb losses or the right to receive benefits from the VIE. If the Company is deemed the primary beneficiary of a VIE, the Company consolidates such entity and reflects the non-controlling interest of other beneficiaries of that entity. If the Company is not the primary beneficiary, no consolidation is necessary, and the Company accounts for the investment or other variable interest in accordance with applicable U.S. GAAP.

Equity Method of Accounting

In circumstances where the Company has the ability to exercise significant influence, but not control, over the operating and financial policies of an entity in which the Company has an investment, the Company utilizes the equity method of accounting for recording related investment activity. In assessing whether the Company exercises significant influence, the Company considers the nature and magnitude of the investment, the voting and protective rights the Company holds, any participation in the governance of the other entity and other relevant factors such as the presence of a collaborative or other business relationship.

Under the equity method of accounting, the Company's investments are initially recorded at cost on the condensed consolidated balance sheets. Upon recording an equity method investment, the Company evaluates whether there are basis differences between the carrying value and fair value of the Company's proportionate share of the investee's underlying net assets. Typically, the Company amortizes basis differences identified on a straight-line basis over the underlying assets' estimated useful lives when calculating the attributable earnings or losses, excluding the basis differences attributable to in-process research and development that had no alternative future use ("IPR&D"). If the Company is unable to attribute all of the basis difference to specific assets or liabilities of the investee, the residual excess of the cost of the investment over the proportional fair value of the investee's assets and liabilities is considered to be Equity Method Goodwill and is recognized within the equity investment balance, which is tracked separately within the Company's memo accounts. The Company subsequently records in the condensed consolidated statements of operations and comprehensive income (loss) its share of income or loss of the other entity within other income/expense. If the share of losses exceeds the carrying value of the Company's investment, the Company will suspend recognizing additional losses and will continue to do so unless it commits to providing additional funding; however, if there are intra-entity profits this can cause the investment balance to go negative.

The Company evaluates its equity method investments for impairment whenever events or changes in circumstance indicate that the carrying amounts of such investments may be impaired and considers qualitative and quantitative factors including the investee's financial metrics, product and commercial outlook and cash usage. If a decline in the value of an equity method

investment is determined to be other than temporary, a loss is recorded in earnings in the current period and the investment is written down to fair value.

At September 30, 2021, the Company accounted for its investment in NewCo under the equity method of accounting and no impairment charges were recognized during the three and nine months ended September 30, 2021. Refer to Note 8 for further details.

Recent Accounting Pronouncements – Adopted

In December 2019, the FASB issued Accounting Standards Update ("ASU") 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which is intended to simplify the accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. The Company adopted ASU 2019-12 on January 1, 2021. The adoption did not have a material effect on the Company's condensed consolidated financial statements.

3. Marketable Securities

The following table summarizes the Company's available-for-sale marketable securities as of September 30, 2021 and December 31, 2020 at net book value:

	September 30, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(In thousands)			
Marketable securities:				
U.S. Treasury and other government securities	$ 251,302	$ 9	$ (69)	$ 251,242
Financial institution debt securities	395,052	12	(66)	394,998
Corporate debt securities	32,099	-	(9)	32,090
Other asset-backed securities	135,702	1	(51)	135,652
Total	$ 814,155	$ 22	$ (195)	$ 813,982

	December 31, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(In thousands)			
Marketable securities:				
U.S. Treasury and other government securities	$ 245,666	$ 13	$ (11)	$ 245,668
Financial institution debt securities	138,445	6	(8)	138,443
Corporate debt securities	41,765	3	(2)	41,766
Other asset-backed securities	11,474	1	(1)	11,474
Total	$ 437,350	$ 23	$ (22)	$ 437,351

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At September 30, 2021 and December 31, 2020, the balance in the Company's accumulated other comprehensive (loss) income was composed of activity related to the Company's available-for-sale marketable securities. There were no realized gains or losses in the nine months ended September 30, 2021 or for the year ended December 31, 2020. The Company did not reclassify any amounts out of accumulated other comprehensive (loss) income during this period. The Company did not have any securities in a material unrealized loss position at September 30, 2021 or December 31, 2020.

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, 2021 and December 31, 2020, 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, 2021 and December 31, 2020, the Company's financial assets recognized at fair value on a recurring basis consisted of the following:

	Fair Value as of September 30, 2021			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents and restricted cash equivalents	$ 335,916	$ 335,916	$ -	$ -
Marketable securities:				
U.S. Treasury and other government securities	251,242	220,670	30,572	-
Financial institution debt securities	394,998	-	394,998	-
Corporate debt securities	32,090	-	32,090	-
Other asset-backed securities	135,652	-	135,652	-
Total marketable securities	813,982	220,670	593,312	-
Total	$ 1,149,898	$ 556,586	$ 593,312	$ -

	Fair Value as of December 31, 2020			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents and restricted cash equivalents	$ 163,805	$ 163,805	$ -	$ -
Marketable securities:				
U.S. Treasury and other government securities	245,668	241,664	4,004	-
Financial institution debt securities	138,443	-	138,443	-
Corporate debt securities	41,766	-	41,766	-
Other asset-backed securities	11,474	-	11,474	-
Total marketable securities	437,351	241,664	195,687	-
Total	$ 601,156	$ 405,469	$ 195,687	$ -

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. After completing its validation procedures, the Company did not adjust or override any fair value measurements provided by the pricing services as of September 30, 2021 or December 31, 2020.

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

The Company's investment in NewCo was recorded at fair value, determined according to Level 3 inputs in the fair value hierarchy described above. Refer to Note 8 for further details.

5. Accrued Expenses

Accrued expenses consisted of the following:

	September 30, 2021	December 31, 2020
	(In thousands)	
Employee compensation and benefits	$ 11,828	$ 10,920
Accrued research and development	7,873	11,008
Accrued legal and professional expenses	2,561	1,876
Accrued other	2,371	1,750
Total accrued expenses	$ 24,633	$ 25,554

6. Commitments and Contingencies

Litigation

There have been no material changes to any of the outstanding litigation, nor is the Company a party to any new litigation, since December 31, 2020, except as described below. 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, 2020.

Caribou Arbitration

On October 17, 2018, the Company initiated an arbitration proceeding against Caribou Biosciences, Inc. ("Caribou") asserting that Caribou violated the terms and conditions of a license agreement the Company entered into with them in July 2014 related to certain IP (the "Caribou License"), as well as other contractual and legal obligations to the Company, by using and seeking to license to third parties two patent families relating to specific structural or chemical modifications of guide RNAs ("gRNAs"), that were purportedly invented or controlled by Caribou, in the Company's exclusive human therapeutic field, before an agreed-upon cutoff date of January 30, 2018.

On September 26, 2019, the Company announced that the arbitration panel issued an interim award concluding that both the structural and chemical gRNA modification technologies were exclusively licensed to the Company by Caribou pursuant to the Caribou License. Nevertheless, the arbitration panel, solely with respect to the clinically modified gRNAs, stated that it will declare that Caribou has an equitable "leaseback", which it described as exclusive, perpetual and worldwide (the "Caribou Award"). The Caribou Award does not include the structural guide modifications IP also at issue in the arbitration, any other IP exclusively licensed or sublicensed by Caribou to the Company under the Caribou License (including but not limited to the foundational CRISPR/Cas9 IP co-owned by the Regents of the University of California, University of Vienna and Dr. Emmanuelle Charpentier), or any other of the Company's IP. On February 6, 2020, the panel clarified that the Caribou Award is limited to a particular on-going Caribou program, known as CB-010, which seeks to develop a CAR-T product directed at CD19.

On June 16, 2021, the Company executed a Leaseback Agreement ("Leaseback") with Caribou, which settled the ongoing arbitration. Under the Leaseback negotiated by the parties, in exchange for an upfront payment, potential future regulatory and sales milestones, and single-digit royalties payable by Caribou, the Company has agreed to leaseback or sublicense certain CRISPR/Cas9 IP, including the Company's 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 the Company's in-licensed IP. The Company recorded $1.0 million within "Collaboration Revenue" in the second quarter of 2021 on the condensed consolidated statements of operations and comprehensive loss for an upfront payment related to the Leaseback and received the payment in the third quarter of 2021.

License Agreements

The Company is party to license agreements, which include contingent payments. These payments will become payable if and when certain development, regulatory and commercial milestones are achieved. As of September 30, 2021, the satisfaction and timing of the contingent payments is uncertain and not reasonably estimable.

7. Collaborations

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, 2021, the Company's accounts receivable and contract liabilities were related to its collaborations with Regeneron Pharmaceuticals, Inc. ("Regeneron"), Novartis Institutes for BioMedical Research, Inc. ("Novartis") and NewCo.

The following table presents changes in the Company's accounts receivable and contract liabilities during the nine months ended September 30, 2021 and 2020 (in thousands):

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Nine Months Ended September 30, 2021				
Accounts receivable	$ 2,130	$ 5,575	$ (5,214)	$ 2,491
Contract liabilities - Deferred revenue	$ 73,931	$ 62,900	$ (17,049)	$ 119,782

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Nine Months Ended September 30, 2020				
Accounts receivable	$ 4,620	$ 102,203	$ (105,606)	$ 1,217
Contract liabilities - Deferred revenue	$ 28,810	$ 87,477	$ (36,673)	$ 79,614

During the nine months ended September 30, 2021 and 2020, the Company recognized the following revenues as a result of changes in the contract liability balance (in thousands):

	Nine Months Ended September 30,	
Revenue recognized in the period from:	**2021**	**2020**
Amounts included in the contract liability at the beginning of the period	$ 16,861	$ 10,249

Costs to obtain and fulfill a contract

The Company did not incur any 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 (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").

On May 30, 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 a missing therapeutic protein, and to overcome the limitations of traditional gene therapy. The collaboration was extended until April 2024, at which point Regeneron has an option to renew for an additional two years. The 2020 Regeneron Amendment also grants 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.

Since December 31, 2020, there have been no material changes to the key terms of the 2016 Regeneron Agreement and the 2020 Regeneron Amendment (the "Amended Agreements"). For further information on the terms and conditions of these agreements, please see the notes to the consolidated financial statements included in the Company's Annual Report for the year ended December 31, 2020.

Revenue Recognition – Collaboration Revenue. Through September 30, 2021, excluding amounts allocated to Regeneron's purchase of the Company's common stock, the Company recorded $145.0 million in upfront payments under the Amended Agreements and $36.6 million for research and development services, primarily under the ATTR Co/Co agreement. Through September 30, 2021, the Company has recognized $141.9 million of collaboration revenue under all arrangements, including $6.7 million and $18.7 million during the three and nine months ended September 30, 2021, respectively, and $22.2 million and $46.4 million during the three and nine months ended September 30, 2020, respectively, in the condensed consolidated statements of operations and comprehensive loss. This includes $2.1 million and $3.9 million during the three and nine months ended September 30, 2021, respectively, and $1.2 million and $9.8 million during the three and nine months ended September 30, 2020, 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 $1.1 million and $2.1 million during the three and nine months ended September 30, 2021, respectively.

As of September 30, 2021, there was approximately $57.1 million of the aggregate transaction price of the Amended Agreements remaining to be recognized, which the Company expects to be recognized during the research term through April 2024.

As of September 30, 2021 and December 31, 2020, the Company had accounts receivable of $2.1 million related to the Amended Agreements. The Company had deferred revenue of $57.1 million and $73.9 million as of September 30, 2021 and December 31, 2020, respectively, related to the Amended Agreements.

License and Collaboration Agreement with New CAR-T Cell Therapy Company ("NewCo")

On July 30, 2021 (the "Effective Date"), the Company entered into two agreements with NewCo: (1) a license and collaboration agreement (the "LCA"), under which the Company will collaborate to develop allogeneic universal CAR-T cell therapies and granted NewCo 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 (2) a co-development and co-funding agreement (the "NewCo Co/Co"), under which the Company will co-develop and co-commercialize allogeneic universal CAR-T cell products for an immuno-oncology indication.

Scope: The Company granted NewCo an exclusive license to combine the Company's CRISPR/Cas9 technology platform with NewCo's switchable, universal CAR-T cell technology platform and made available to NewCo certain know-how and materials. For an eighteen-month period after the Effective Date, the Company will provide to NewCo any improvements with respect to the underlying technology that are developed. For the two-year period immediately following the Effective Date, the Company will perform certain activities, at the Company's cost and expense, including providing to NewCo certain know-how and materials to enable NewCo to use the Company's CRISPR/Cas9 technology platform, as well as making available employees with requisite knowledge and experience to provide advice and answer questions regarding such know-how and materials for a limited number of hours per year (the "Knowledge Transfer Period"). In addition, the Company and NewCo will collaborate on at least seven universal CAR-T cell products that combine the Company's allogeneic T cell technology with NewCo's switchable, universal CAR-T cell technology, referred to as the ("Allo Collaboration").

NewCo will pay the Company to provide supply and manufacturing services for them, including supplying good manufacturing practice CRISPR reagents to support the research and development of all CRISPR Products (as defined in the LCA) under the Allo Collaboration until the completion of the first Pivotal Trial (as defined in the LCA) of the first such CRISPR Product.

Financial Terms: In exchange for the license, the Company received a 33.33% equity interest in NewCo at the time of the initial closing.

Governance: The parties formed a joint steering committee ("JSC"), which is responsible for setting research objectives and overseeing the general strategies and research and development activities undertaken by the parties under the LCA. The JSC will meet quarterly until the expiration or termination of the Allo Collaboration.

Term and Termination: The term of the Allo Collaboration is from the Effective Date of the LCA until the completion of all activities under the then-current Allo Collaboration with respect to all relevant CRISPR Products. The LCA contains termination provisions, including termination for insolvency, material breach, patent challenge, convenience, and cessation.

Co-Development and Co-Promotion Agreement: Under the NewCo Co/Co the parties will co-develop and co-commercialize in the U.S. and key European countries certain allogeneic universal CAR-T products directed to an immuno-oncology target. The Company is the lead commercialization party in the U.S., and NewCo is the lead commercialization party in the European countries. The parties will share equally in the profits and development costs. The Company will have one additional option to enter into a second co-development and co-funding agreement from selected allogeneic universal CAR-T cell therapy products that the parties intend to develop under the Allo Collaboration for a payment of $30.0 million to NewCo.

Accounting Analysis: The Company concluded that the accounting treatment for the LCA is within the scope of ASU 2014-09, *Revenue from Contracts with Customers (Topic 606)*, and its related amendments (collectively known as "ASC 606"). The Company evaluated the promised goods and services under the LCA and determined that it included one performance obligation: a combined performance obligation including the license to the allogeneic technology, initial know-how and ongoing support services, including participation in the JSC during the two-year Knowledge Transfer Period.

The transaction price was determined to be $62.9 million, which represents the fair value of the Company's equity stake in NewCo as of the Effective Date. The Company will allocate the full transaction price to the combined performance obligation including the license to allogeneic technology, the JSC, initial-know-how and ongoing support services. The Company will recognize the $62.9 million using a time elapsed input method over the Knowledge Transfer Period, which in management's judgement, is the best measure of progress towards satisfying the performance obligation as this method provides the most faithful depiction of the entity's performance in transferring control of the goods and services promised to NewCo. This represents the Company's best estimate of the obligation, as after this period NewCo will be able to fully benefit from the licensed IP on its own or with readily available resources. Revenue recorded during each period will be eliminated by an amount representing the Company's 33.33% ownership interest in NewCo at that time, as this represents the intra-entity profit related to the transaction. The Company will re-evaluate the measure of progress in each reporting period and, if necessary, adjust the measure of performance and related revenue recognition. The Company completed the initial transfer of know-how in the third quarter of 2021. The Company recognized $125.0 thousand in revenue for the three and nine months ended September 30, 2021 and eliminated $62.5 thousand in intra-entity profits, which should be deferred until realized by NewCo. The deferral will be recognized if and when NewCo commercializes a product with the Company's license or abandons the related project. Until such time, the $62.5 thousand of revenue is indefinitely deferred and excluded from the results of operations of the Company.

As of September 30, 2021 the Company had deferred revenue of $62.7 million related to the NewCo LCA.

The payments attributable to the supply and manufacturing services are variable and are commensurate with the standalone selling prices of the services, and as such, will be attributed to those services. The Company did not record any consideration related to the supply and manufacturing services during the third quarter of 2021.

NewCo Co/Co - Accounting Analysis: The Company concluded that the NewCo Co/Co agreement meets the definition of a collaborative arrangement per ASC 808, *Collaborative Arrangements* ("ASC 808"), which is outside of the scope of ASC 606. Since ASC 808 does not provide recognition and measurement guidance for collaborative arrangements, the Company has analogized to ASC 606. As such, the Company classifies cumulative amounts paid or received under the cost sharing provisions of the NewCo Co/Co as a component of revenues in the condensed consolidated statements of operations and comprehensive loss, to the extent that this does not result in a cumulative "negative revenue" amount, in which case the cumulative shortfall would be reclassified as an expense. The Company has recognized $0.2 million in revenues related to the NewCo Co/Co agreement for the three and nine months ended September 30, 2021.

Novartis Institutes for BioMedical Research, Inc.

In December 2014, the Company entered into a strategic collaboration agreement with Novartis (the "2014 Novartis Agreement"), primarily focused on the research of new *ex vivo* CRISPR/Cas9-edited therapies using CAR-T cells and hematopoietic stem cells ("HSCs"). The agreement was amended in December 2018 (the "Novartis Amendment") to also include research on ocular stem cells ("OSCs"). In December 2019, per the terms of the 2014 Novartis Agreement, the research term ended, although the 2014 Novartis Agreement remains in effect, for which the Company will be eligible to receive milestone and royalty payments in the future. In June 2021, the Company entered into Amendment No. 3 (the "Amendment") to the 2014

Novartis Agreement. The Amendment amends Novartis' rights with respect to all of the CAR-T Therapeutic Targets (as defined in the 2014 Novartis Agreement) that Novartis selected under the 2014 Novartis Agreement, including (a) making Novartis' license non-exclusive for such CAR-T Therapeutic Targets, (b) removing Novartis' diligence and related reporting obligations for such CAR-T Therapeutic Targets, and (c) refining the scope of Novartis' sublicense rights for such CAR-T Therapeutic Targets. The Company made a one-time payment to Novartis of $10.0 million within 30 days after the effective date of the Amendment, which was recorded as research and development expense in the condensed consolidated statements of operations and comprehensive loss for the three and nine months ended September 30, 2021. Since December 31, 2020, there have been no other material changes to the key terms of the 2014 Novartis Agreement and the Novartis Amendment. For further information on the terms and conditions of these agreements, please see the notes to the consolidated financial statements included in the Company's Annual Report for the year ended December 31, 2020.

Revenue Recognition – Milestone: In March 2020, the U.S. Food and Drug Administration ("FDA") accepted the investigational new drug ("IND") application submitted by Novartis for a CRISPR/Cas9-based engineered cell therapy for the treatment of sickle cell disease. As a result of meeting this milestone, the Company recognized $5.0 million as collaboration revenue within the condensed consolidated statement of operations and comprehensive loss. In September 2021, an additional milestone was reached and, as a result, the Company recognized $0.3 million as collaboration revenue within the condensed consolidated statement of operations and comprehensive loss. No other milestones under the 2014 Novartis Agreement and the Novartis Amendment were achieved during the three or nine months ended September 30, 2021 or 2020. The Company is eligible to receive additional downstream success-based milestones and royalties.

As of September 30, 2021, the Company had a $0.3 million account receivable related to the milestone noted above and no deferred revenue related to the 2014 Novartis Agreement and the Novartis Amendment. As of December 31, 2020, the Company had no accounts receivable or deferred revenue related to the 2014 Novartis Agreement and the Novartis Amendment.

8. Equity-Method Investment

On July 30, 2021, the Company finalized a transaction in which the Company, Cellex and BXLS established NewCo, 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 NewCo for a 33.33% equity interest in NewCo 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, NewCo through its noncontrolling representation on NewCo's Board of Directors and the Company's equity interest in NewCo. 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 NewCo that most significantly impact NewCo's economic performance. Accordingly, the Company does not consolidate the financial statements of NewCo and accounts for its investment using the equity method of accounting.

As of July 30, 2021, the closing date, the fair value of the Company's investment in NewCo was $62.9 million which represents the fair value of the Preferred Stock received in exchange for the exclusive license to the Company's CRISPR/Cas9 allogeneic platform (See Note 7). In determining the fair value of the Company's investment, the Company used an option pricing model which requires the input of certain subjective assumptions. The key assumptions used in the option pricing model, which are level 3 inputs, include the anticipated holding period to an exit and liquidity event, the volatility of market participants (76%), the probability of NewCo achieving certain milestones to obtain subsequent financings (75%) and the discount for lack of marketability (11%).

Due to the timing and availability of financial information of NewCo, the Company will record its share of losses from NewCo on a quarterly basis on a one-quarter lag from July 30, 2021. Therefore, the Company will record its share of two months of NewCo's losses generated in the third quarter of 2021 in the Company's operating results in the fourth quarter of 2021. The Company is not aware of any material events or transactions during this period. The Company's initial investment in NewCo was $62.9 million. The elimination of the intra-entity profit component of $0.1 million (See Note 7) resulted in a reduction in the balance of the investment in NewCo, bringing the carrying value of the investment to $62.8 million as of September 30, 2021. The excess of the initial fair value of the Company's investment over the underlying equity in the carrying value of the net assets of NewCo has not yet been allocated. The Company expects to complete the allocation in the fourth quarter of 2021.

At September 30, 2021, the maximum exposure to loss is limited to the Company's equity investment in the joint venture.

9. Leases

In March 2020, the Company entered into an agreement to lease approximately 39,000 square feet of office and laboratory space at 281 Albany Street in Cambridge, Massachusetts under an operating lease agreement (the "281 Albany Lease"). The Company's obligation to pay rent will start on the date that is six months after the commencement date or the date on which the Company occupies the premises, whichever occurs earlier (the "Rent Commencement Date"). The initial term of the 281 Albany Lease is ten years following the Rent Commencement Date. In March 2021 the Company determined, in accordance with ASC 842, *"Leases (Topic 842)"* ("ASC 842"), that the commencement date of the lease had been met as the facility was substantially complete and available for use and, accordingly, the Company recognized a right-of-use asset and a lease liability of approximately $40.4 million and $34.8 million, respectively, in the first quarter of 2021 related to the 281 Albany Lease. In determining the lease liability, the Company used an incremental borrowing rate of 5.52% based on a number of factors including the Company's credit rating and the lease term. Included in the recognized right-of-use asset at the inception of the lease was approximately $5.6 million in lease payments that were prepaid under the terms of the lease. The base rent under the 281 Albany Lease is $99.00 per square foot per year during the first year of the term, which is subject to scheduled annual increases up to $128.87 per square foot per year during the last year of the initial term, plus certain operating expenses and taxes. In addition, the landlord agreed to contribute an aggregate of $4.4 million toward the cost of construction and tenant improvements for the premises. In accordance with the 281 Albany Lease, the Company is required to maintain a letter of credit in the amount of $1.9 million that is restricted for the term of the lease. These restricted cash equivalents are reported in "Other Assets" in the Company's condensed consolidated balance sheets. The Company has the option to extend the 281 Albany Lease for two successive five-year terms. The option for this extension is not included as part of the lease liability and right-of-use asset at September 30, 2021, as it is not reasonably certain that it will be exercised.

In July 2021, the Company entered into an agreement to lease 13,662 square feet of office space at 17 Tudor Street in Cambridge, Massachusetts under an operating lease agreement (the "17 Tudor Lease"). The Company's obligation to pay rent will start on November 1, 2021. The initial term of the 17 Tudor Lease is five years and the Company has an option to extend the 17 Tudor Lease for one three-year term. The option for this extension is not included as part of the lease liability and right-of-use asset at September 30, 2021, as it is not reasonably certain that it will be exercised. The base rent under the 17 Tudor Lease is $74.00 per square foot during the first year of the term, which is subject to scheduled annual increases throughout the term, resulting in a base rent of $83.29 per square foot during the last year of the initial term, plus certain operating expenses and taxes. In September 2021 the Company determined, in accordance with ASC 842, that the commencement date of the lease had been met as the Company had gained access to the facility in order to begin work on lessee-owned tenant improvements and, accordingly, the Company recognized a right-of-use asset and a lease liability of approximately $4.9 million in the third quarter of 2021 related to the 17 Tudor Lease. In determining the lease liability, the Company used an incremental borrowing rate of 4.15% based on a number of factors including the Company's credit rating and the lease term. In accordance with the 17 Tudor Lease, the Company is required to maintain a letter of credit in the amount of $0.2 million that is restricted for the term of the lease. These restricted cash equivalents are reported in "Other Assets" in the Company's condensed consolidated balance sheet.

In July 2021, the Company entered into an agreement to extend an existing lease for a clean room located in Waltham, Massachusetts under an operating lease agreement (the "Waltham Lease") for an additional two years. The Company determined, in accordance with ASC 842, that the extension should be accounted for as a lease modification and, accordingly, recorded an adjustment to the right-of-use asset and lease liability of approximately $2.5 million in the third quarter of 2021 related to the Waltham Lease.

10. Equity-Based Compensation

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, 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. Stock options granted under the 2015 Plan generally vest 25% on the first anniversary of the original vesting date, with the balance vesting monthly over the remaining three years, unless they contain specific performance-based vesting provisions. The maximum term of stock options granted under the 2015 Plan is ten years.

As of September 30, 2021, there were 3,787,307 shares available for future issuance under the 2015 Plan and the 2016 Employee Stock Purchase Plan. The number of shares reserved for issuance under the 2015 Plan shall be cumulatively increased by four percent of the number of shares of common stock issued and outstanding on the immediately preceding December 31 or such lesser number of shares of common stock as determined by the board of directors. The number of shares reserved for issuance

under the 2016 Employee Stock Purchase Plan shall be cumulatively increased by the lesser of a) one percent of the number of shares of common stock issued and outstanding on the immediately preceding December 31, b) 500,000 shares of common stock, or c) such lesser number of shares of common stock as determined by the board of directors.

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,	
	2021	2020	2021	2020
	(In thousands)			
Research and development	$ 9,017	$ 2,775	$ 18,643	$ 7,325
General and administrative	6,393	2,625	13,805	6,996
Total	$ 15,410	$ 5,400	$ 32,448	$ 14,321

Restricted Stock Units

RSUs are measured at fair value based on the quoted price of the Company's common stock.

The following table summarizes the Company's restricted stock activity for the nine months ended September 30, 2021:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Unvested restricted stock units as of December 31, 2020	193,936	$ 23.98
Granted	354,072	63.13
Vested	(50,946)	17.80
Cancelled	(53,777)	38.02
Unvested restricted stock units as of September 30, 2021	443,285	$ 54.26

In March 2021, the Company granted 259,839 RSUs with a service condition to employees as part of their annual grant, which vest over a period of four years. The weighted average grant date fair value of these RSUs was $57.71. The vesting start date for these RSUs is January 1, 2021.

Shares vesting during the nine months ended September 30, 2021 included 26,235 shares that vested in June 2021 as a service condition was met and 21,430 shares that were accelerated in September 2021 based on the Company reaching a performance milestone. Included in the unvested restricted stock as of September 30, 2021 are 42,860 RSUs that include a performance condition in addition to a service condition. These RSUs would vest over a period of 1.2 years and were subject to accelerated vesting based on the Company's programs achieving certain development milestones before December 1, 2022. In October 2021, these development milestones were achieved and, accordingly, the vesting of the RSUs was accelerated during the fourth quarter of 2021. The fair value of the RSUs at date of grant was $15.05.

As of September 30, 2021, there was $19.9 million of unrecognized equity-based compensation expense related to restricted stock that is expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 2.8 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 $105.17 and $50.73 per option for those options granted during the three and nine months ended September 30, 2021 and $13.38 and $8.55 per option for those options granted during the three and nine months ended September 30, 2020, respectively. 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, 2021 was $171.3 million and $255.8 million, respectively, and during the three and nine months ended September 30, 2020 was $0.9 million and $1.7 million, respectively. Weighted average assumptions used to apply this pricing model were as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Risk-free interest rate	1.0%	0.4%	0.9%	0.9%
Expected life of options	6.0 years	6.0 years	6.0 years	5.5-6.0 years
Expected volatility of underlying stock	75.2%	70.8%	72.7%	67.6%
Expected dividend yield	0.0%	0.0%	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 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.

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 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.

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, 2021:

	Number of Options	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
			(In years)	(In thousands)
Outstanding at December 31, 2020	6,977,440	$ 15.43		
Granted	2,435,102	79.17		
Exercised	(2,636,437)	15.12		
Forfeited	(559,241)	29.80		
Outstanding at September 30, 2021	6,216,864	$ 39.23	8.01	$ 601,927
Exercisable at September 30, 2021	1,977,984			

As of September 30, 2021, there was $120.8 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 3.2 years.

11. Loss Per Share

The Company calculates basic loss per share by dividing net loss for each respective period by the weighted average number of common shares outstanding for each respective period. The Company computes diluted loss per share after giving consideration to the dilutive effect of stock options and unvested restricted stock 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,	
	2021	2020	2021	2020
	(In thousands)			
Net loss	$ (71,644)	$ (27,840)	$ (186,655)	$ (92,039)
Weighted average shares outstanding, basic and diluted	73,706	58,754	69,720	54,218
Net loss per share, basic and diluted	$ (0.97)	$ (0.47)	$ (2.68)	$ (1.70)

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,	
	2021	2020
	(In thousands)	
Unvested restricted stock units	443	225
Stock options	6,217	7,527
	6,660	7,752

12. Stockholders' Equity

The following tables present changes in stockholders' equity for the nine-month periods ended September 30, 2021 and 2020 (in thousands, except share data):

	Common		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Income (Loss)	Deficit	Equity
Balance at December 31, 2020	66,234,056	$ 7	$ 962,173	$ 1	$ (435,109)	$ 527,072
Issuance of common stock through at-the-market offerings, net of issuance costs of $52	641,709	-	45,255	-	-	45,255
Exercise of stock options	1,014,569	-	13,340	-	-	13,340
Equity-based compensation	-	-	6,424	-	-	6,424
Other comprehensive loss	-	-	-	(13)	-	(13)
Net loss	-	-	-	-	(46,205)	(46,205)
Balance at March 31, 2021	67,890,334	7	1,027,192	(12)	(481,314)	545,873
Exercise of stock options	394,801	-	6,163	-	-	6,163
Vesting of restricted stock units	26,235	-	-	-	-	-
Issuance of shares under employee stock purchase plan	20,410	-	970	-	-	970
Equity-based compensation	-	-	10,614	-	-	10,614
Other comprehensive loss	-	-	-	(1)	-	(1)
Net loss	-	-	-	-	(68,806)	(68,806)
Balance at June 30, 2021	68,331,780	7	1,044,939	(13)	(550,120)	494,813
Issuance of common stock through follow-on offering, net of issuance costs of $284	4,758,620	-	648,315	-	-	648,315
Exercise of stock options	1,227,067	-	20,365	-	-	20,365
Vesting of restricted stock units	24,711	-	-	-	-	-
Equity-based compensation	-	-	15,410	-	-	15,410
Other comprehensive loss	-	-	-	(161)	-	(161)
Net loss	-	-	-	-	(71,644)	(71,644)
Balance at September 30, 2021	74,342,178	$ 7	$ 1,729,029	$ (174)	$ (621,764)	$ 1,107,098

	Common		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Income	Deficit	Equity
Balance at December 31, 2019	50,198,044	$ 5	$ 570,493	$ 261	$ (300,878)	$ 269,881
Issuance of common stock through at-the-market offerings, net of issuance costs of $48	351,252	-	5,079	-	-	5,079
Exercise of stock options	53,579	-	336	-	-	336
Equity-based compensation	-	-	4,157	-	-	4,157
Other comprehensive income	-	-	-	112	-	112
Net loss	-	-	-	-	(31,806)	(31,806)
Balance at March 31, 2020	50,602,875	5	580,065	373	(332,684)	247,759
Issuance of common stock through follow-on offering, net of issuance costs of $369	6,301,370	1	107,731	-	-	107,732
Issuance of common stock in private placement with Regeneron	925,218	-	12,580	-	-	12,580
Issuance of common stock through at-the-market offerings, net of issuance costs of $23	755,848	-	9,643	-	-	9,643
Exercise of stock options	83,631	-	1,035	-	-	1,035
Issuance of shares under employee stock purchase plan	55,296	-	685	-	-	685
Equity-based compensation	-	-	4,764	-	-	4,764
Other comprehensive loss	-	-	-	(218)	-	(218)
Net loss	-	-	-	-	(32,393)	(32,393)
Balance at June 30, 2020	58,724,238	6	716,503	155	(365,077)	351,587
Exercise of stock options	67,974	-	597	-	-	597
Equity-based compensation	-	-	5,400	-	-	5,400
Other comprehensive loss	-	-	-	(124)	-	(124)
Net loss	-	-	-	-	(27,840)	(27,840)
Balance at September 30, 2020	58,792,212	$ 6	$ 722,500	$ 31	$ (392,917)	$ 329,620

Follow-on Offering

On June 29, 2021, the Company entered into an underwriting agreement related to a public offering of 4,758,620 shares of its common stock (inclusive of shares sold pursuant to the exercise of the underwriters' option to purchase additional shares) at a public offering price of $145.00 per share. The offering closed on July 2, 2021, for aggregated net proceeds of $648.3 million after deducting $41.7 million in underwriting discounts and offering costs.

At-the-Market Offering Programs

In August 2019, the Company entered into an Open Market Sale Agreement (the "2019 Sales Agreement") with 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 Sales Agreement. Please refer to the Company's Annual Report for the year ended December 31, 2020 for additional information regarding these offerings.

During the first half of 2021, the Company issued 641,709 shares of its common stock in a series of sales at an average price of $72.79 per share in accordance with the 2019 Sales Agreement, for aggregate net proceeds of $45.3 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. There was no activity under the 2019 Sales Agreement in the third quarter of 2021. During the nine months ended September 30, 2020, the Company issued 1,107,100 shares of its common stock in a series of sales at an average price of $13.78 per share in accordance with the 2019 Sales Agreement, for aggregate net proceeds of $14.7 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, 2021, $47.4 million in shares of common stock remain eligible for sale under the 2019 Sales Agreement.

13. 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.

14. Subsequent Events

In October 2021, the Company and SparingVision SAS ("SparingVision"), a genomic medicine company developing vision saving treatments for ocular diseases, announced a strategic collaboration to develop novel genomic medicines utilizing CRISPR/Cas9 technology for the treatment of ocular diseases. The Company will grant SparingVision exclusive rights to its proprietary *in vivo* CRISPR/Cas9-based genome editing technology for up to three ocular targets addressing diseases with significant unmet medical need. SparingVision will lead and fund the preclinical and clinical development for the genome editing product candidates pursued under the collaboration. In addition, the parties will research and develop novel self-inactivating adeno-associated virus ("AAV") vectors and lipid nanoparticle-based approaches to address delivery of CRISPR/Cas9 genome editing reagents to the retina. The Company will receive a 10% equity ownership stake in SparingVision. The Company will also be eligible to receive certain development and commercial milestone payments (up to approximately $200 million per product) as well as royalties on potential future sales of products arising from the collaboration. The Company will have an option to obtain exclusive U.S. commercialization rights for product candidates arising from two of three collaboration targets. For product candidates the Company chooses to option, it will pay an opt-in fee, reimburse certain costs, share in 50% of development costs and pay royalties to SparingVision on U.S. sales.

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 amyloidosis, including the ability to successfully complete our Phase 1 study and determine a recommended dose in our ongoing Phase 1 study that can be advanced into later-stage studies, or the success of such program;
- the anticipated timing of our clinical trial and initiating patient screening for NTLA-5001, our program for the treatment of acute myeloid leukemia, or the success of such program;
- the anticipated timing of our clinical trial and initiating enrollment for NTLA-2002, our program for the treatment of hereditary angioedema, or the success of such program;
- our ability to use a modular platform capability or other strategies to efficiently discover and develop product candidates, including by applying learnings from one program to other programs;
- our ability to research, develop or maintain a pipeline of product candidates, including *in vivo* and *ex vivo* product candidates, including allogeneic *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, effective, pure and potent 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;
- the effect of the ongoing COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations; 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 novel, potentially curative therapeutics using CRISPR/Cas9 technology. 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, we are pursuing two primary approaches. Our *in vivo* programs use intravenously administered CRISPR as the therapy, in which our proprietary delivery technology enables highly precise editing of disease-causing genes directly within specific target tissues. Our *ex vivo* programs use CRISPR to create the therapy by using engineered human cells to treat cancer and autoimmune diseases. Our deep scientific, technical and clinical development experience, along with our robust intellectual property ("IP") portfolio, enables us to unlock broad therapeutic applications of CRISPR/Cas9 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, 2020.

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 build 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. 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 CRISPR/Cas9 is the tool that creates the engineered cell therapy. All of our revenue to date has been collaboration revenue. Since our inception and through September 30, 2021, we have raised an aggregate of approximately $1,815.7 million to fund our operations, of which $276.8 million was through our collaboration agreements, $170.5 million was from our initial public offering and concurrent private placements, $1,086.9 million was from follow-on public offerings, $196.5 million was from at-the-market offerings and $85.0 million was from the sale of convertible preferred stock.

Our lead *in vivo* candidate, NTLA-2001 for the treatment of transthyretin ("ATTR") amyloidosis, is the first CRISPR/Cas9-based therapy candidate to be administered systemically, via intravenous infusion, for precision editing of a gene in a target tissue in humans. In parallel, we are developing *ex vivo* applications to address immuno-oncology and autoimmune diseases, where CRISPR/Cas9 is the tool that creates the engineered cell therapy. Our most advanced *ex vivo* programs include a wholly owned T cell receptor ("TCR")-T cell candidate, NTLA-5001 for the treatment of acute myeloid leukemia ("AML"), and a program with Novartis Institutes for BioMedical Research, Inc. ("Novartis") to engineer hematopoietic stem cells ("HSCs") for the treatment of sickle cell disease.

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 single knockout, repair 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, hereditary angioedema ("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

Background

ATTR amyloidosis is a progressive and fatal disorder resulting from deposition of insoluble amyloid fibrils into multiple organs and tissues leading to systemic failure. Blood-borne transthyretin ("TTR") protein is produced by hepatocytes and normally circulates as a soluble homotetramer that facilitates transport of vitamin A, via retinol binding protein, as well as the thyroid hormone, thyroxine. Mutations in the *TTR* gene lead to the production of TTR proteins that are destabilized in their tetramer form. These tetramers more readily dissociate into the monomeric form, and thence to an aggregative form that results in amyloid deposits in tissues. These deposits cause damage in those tissues, resulting in a disorder known as hereditary TTR amyloidosis ("ATTRv"). Over 120 different genetic mutations are currently known to cause ATTRv.

Deposits of TTR amyloid in the heart, nerves and/or other tissues can lead to diverse disease manifestations, including two main hereditary forms – ATTRv with polyneuropathy ("ATTRv-PN") and ATTRv with cardiomyopathy ("ATTRv-CM"). Typical onset of disease symptoms is during adulthood and can be fatal within two to 15 years. Estimates suggest that approximately 50,000 patients suffer from ATTRv worldwide.

In addition to the hereditary forms described above, ATTR amyloidosis can also develop spontaneously in the absence of any *TTR* gene mutation. This wild-type ATTR ("ATTRwt") is increasingly being recognized as a significant and often undiagnosed cause of heart failure in the elderly and is the subject of active investigation. Recent estimates suggest that, globally, between 200,000 and 500,000 people may suffer from ATTRwt with cardiomyopathy ("ATTRwt-CM").

In non-human primate ("NHP") studies, we have demonstrated our ability to reduce circulating TTR protein to estimated therapeutically relevant levels after a single systemic administration of LNPs containing our CRISPR/Cas9 complex. In December 2019, we completed a year-long durability study of our lead LNP formulation, maintaining an average reduction of more than 95% of serum TTR protein after a single dose in NHPs. The data from our various NHP studies has shown that following editing, our proprietary modular LNP delivery system is rapidly cleared from circulation, such that exposure to components is transient and all CRISPR/Cas9 complex is undetectable in blood within 14 days of administration.

About the NTLA-2001 Clinical Program

In November 2020, we announced that the first patient had been dosed with NTLA-2001, our lead *in vivo* genome editing candidate which we are developing as a single-dose treatment for ATTR amyloidosis, in our Phase 1 study. We are conducting our Phase 1 study to evaluate NTLA-2001 for ATTRv-PN patients. Our first patient was dosed in the United Kingdom ("U.K.") pursuant to authorization of our Clinical Trial Application ("CTA"), which was received from the U.K.'s Medicines and Healthcare products Regulatory Agency ("MHRA") in October 2020. In November 2020, as part of our ongoing Phase 1 study for NTLA-2001, we received a second CTA authorization from New Zealand's Medicines and Medical Device Safety Authority ("MEDSAFE") to enroll ATTR amyloidosis patients at a clinical site. As part of our ongoing development strategy, we are submitting additional regulatory applications in other countries. In March 2021, we announced that the European Commission ("EC") granted orphan drug designation to NTLA-2001. In October 2021, we announced that NTLA-2001 received Orphan Drug Designation from the U.S. Food and Drug Administration ("FDA").

Our global Phase 1 trial is an open-label, multi-center, two-part study of NTLA-2001 in adults with ATTRv-PN. The trial's primary objectives are to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of NTLA-2001. Patients receive a single dose of NTLA-2001 via intravenous administration. The study will enroll up to 38 participants (ages 18-80 years) and consist of a single-ascending dose phase in Part 1 and, following the identification of a recommended dose, an expansion cohort in Part 2.

On June 26, 2021, at the Peripheral Nerve Society ("PNS") Annual Meeting and in the New England Journal of Medicine, we publicly disclosed positive interim data from our ongoing Phase 1 clinical study of NTLA-2001. The interim data cover the first six ATTRv-PN patients across two single-ascending dose cohorts of the Phase 1 study, which is currently being conducted in the U.K. and New Zealand. Single doses of either 0.1 mg/kg or 0.3 mg/kg of NTLA-2001 were administered systemically. Reductions in serum TTR levels were measured from baseline to day 28. Treatment with NTLA-2001 led to dose-dependent reductions in serum TTR, with mean reductions of 52% among the three patients in the 0.1 mg/kg dose group, and 87% among the three patients in the 0.3 mg/kg dose group, including one patient with a 96% reduction.

At both dose levels, NTLA-2001 was generally well-tolerated by the six patients included in the interim analysis, with no serious adverse events or abnormal coagulation or liver findings by day 28. NTLA-2001 is completing the dose-escalation portion of the study, to determine the recommended dose for evaluation in Part 2 of the study, a single-dose expansion cohort. For the third cohort in the dose-escalation portion, we will be evaluating NTLA-2001 at the 1 mg/kg dose level. During the third quarter, to more fully elucidate the dose-response relationship, we began dosing subjects in Cohort 4, evaluating NTLA-2001 in patients with ATTRv-PN at the 0.7 mg/kg dose level. We also accelerated the evaluation of NTLA-2001 for the treatment of patients with transthyretin amyloidosis with cardiomyopathy ("ATTR-CM"). We are in discussions with regulatory authorities on a protocol amendment to expand the Phase 1 trial population to include patients with ATTR-CM.

We plan to present interim data from all four cohorts in the single-ascending dose phase in Part 1 at a company-sponsored event and to initiate Part 2, a single-cohort expansion, in the first quarter of 2022. Data to be presented will include safety and serum TTR knockdown for Cohorts 3 and 4 as well as an early look at durability across all cohorts.

NTLA-2001 is part 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 amyloidosis program. For more information regarding our collaboration with Regeneron, see the section below entitled "**Collaborations - *Regeneron*".**

Hereditary Angioedema ("HAE") Program

Background

HAE is a rare genetic disorder characterized by recurrent, painful and unpredictable episodes of severe swelling. The most common areas of the body to develop swelling are the limbs, face, intestinal tract and airway. Minor trauma or stress may trigger an attack but swelling often occurs without a known trigger. Episodes involving the intestinal tract cause severe abdominal pain, nausea and vomiting. Swelling in the airway can restrict breathing and lead to life-threatening obstruction of the airway. The disease is caused by increased levels of bradykinin, a protein which leads to swelling. Most patients with HAE have a deficiency of C1 esterase inhibitor ("C1-INH") protein, which normally prevents the unregulated release and buildup of bradykinin. HAE is estimated to affect 1 in 50,000 people, with an estimated 11,000 to 21,500 diagnosed HAE patients in the U.S. and Europe.

Currently, there are multiple therapies approved to treat HAE, including acute and prophylactic approaches. Acute treatments are used to treat patients who are experiencing an attack. Prophylactic treatments are used to reduce the number of attacks that a patient may experience. Prophylactic treatments have proven to be effective in reducing the number of attacks for patients, though these treatments either require regular injections that can be associated with significant treatment burden and impact on quality of life or require daily oral therapy that offers incomplete reduction in attack rate compared to injectable therapy.

Using our modular LNP delivery system, we aim to knock out the *kallikrein B1 ("KLKB1"*) gene with a single dose of treatment to permanently reduce the plasma kallikrein protein and activity and thereby ameliorate the frequency and intensity of HAE attacks. We expect our approach should eliminate the current, significant treatment burden for people living with HAE and minimize the risk of breakthrough attacks with extensive and continuous reduction in plasma kallikrein activity. We believe *KLKB1* knockout to be safe, as humans with prekallikrein deficiency appear to have no known health effects. In addition, inhibition of kallikrein activity has proven to be clinically effective as a prophylactic treatment for HAE.

NTLA-2002 is our wholly owned development candidate for the treatment of HAE. In March 2021, we presented preclinical results confirming greater reductions in serum kallikrein protein levels and activity versus the current standard of care for HAE, sustained over seventeen months following a single dose in an ongoing NHP study. Additionally, we presented data from a humanized KLKB1 mouse model of bradykinin-mediated vascular permeability, establishing that a single administration of NTLA-2002 prevented captopril-induced vascular leakage. These results affirm NTLA-2002's therapeutic hypothesis of preventing HAE attacks. In October 2021, we announced the authorization of our CTA by New Zealand's MEDSAFE to initiate our Phase 1/2 study. Additionally, a CTA has been subsequently authorized by the U.K.'s MHRA.

The Phase 1/2 study will evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of NTLA-2002 in adults with Type I or Type II HAE. This includes the measurement of kallikrein protein levels and activity as determined by HAE attack rate measures. The Phase 1 portion of the study is an open-label, single-ascending dose design used to identify up to two dose levels of NTLA-2002 that will be further evaluated in the randomized, placebo-controlled Phase 2 portion of the study. This Phase 1/2 study will identify the dose of NTLA-2002 for use in future studies. We plan to enroll our first patient in the Phase 1 study by the end of 2021.

Alpha-1 Antitrypsin Deficiency ("AATD") Program

Background

AATD is a genetic disorder that results in increased risk for lung and/or liver disease. Alpha-1 antitrypsin ("A1AT"), which is encoded by the *SERPINA1* gene, is a serine protease inhibitor that is primarily produced in the liver and has a wide range of biological functions, one of which is to inhibit neutrophil elastase. Patients with AATD have genetic variants of A1AT which cause the enzyme to accumulate in the liver, reducing the amount of functioning A1AT in the bloodstream. This has two prominent potential downstream clinical manifestations. The first is an increased risk for progressive liver disease, resulting from an accumulation of mutant A1AT enzyme in the liver. The second, and more common, effect is enhanced risk for emphysema resulting from reduced inhibition of neutrophil elastase in the lungs. Both clinical manifestations are progressive and potentially fatal.

It is estimated that there are approximately 250,000 individuals globally and 60,000 in the U.S. with the ZZ genotype, the genotype most associated with AATD and the downstream clinical manifestations. There are another 1.25 million individuals globally estimated to have the SZ genotype, who are also at enhanced risk of developing AATD. While augmentation therapy is available for the treatment of AATD, the effect on pulmonary exacerbations and on the progression of emphysema in AATD has not been conclusively demonstrated in randomized, controlled clinical trials. Also, at present, there are no therapies that have been approved for the treatment of liver disease resulting from AATD.

In October 2021, we announced the nomination of NTLA-3001, our wholly owned development candidate for the treatment of AATD. NTLA-3001 is our first CRISPR/Cas9 mediated *in vivo* gene insertion development candidate. It is designed with the aim to precisely insert a functional *SERPINA1* gene, which encodes the A1AT protein in the liver, with the potential to permanently restore expression of functional A1AT protein levels after a single dose. This approach aims to address AATD-associated lung disease and eliminate the need for sub-optional weekly IV infusions of A1AT augmentation therapy or transplant in severe cases.

In October 2021, we presented data showing that insertion of a healthy form of the *SERPINA1* gene led to normal human A1AT levels in NHPs which were durable through 52 weeks in an ongoing study. We are advancing towards IND-enabling activities for this program and continuing to explore additional editing strategies for AATD.

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, primary hyperoxaluria type 1, as well as other liver targets, which are worked on both independently and in partnership with Regeneron, which leverage our capabilities to knockout, insert and make consecutive edits to the genome. In the third quarter of 2021, we and Regeneron, the lead party, nominated a *Factor 9 ("F9"*) gene insertion development candidate for our Hemophilia B ("Hem B") program, leveraging our jointly developed targeted transgene insertion capabilities to insert *F9*. *F9* is a gene that encodes for Factor IX ("FIX"), a blood-clotting protein that is missing or defective in Hem B patients. In preclinical studies, the companies demonstrated the first CRISPR/Cas9-mediated targeted transgene insertion in the liver of NHPs, which resulted in circulating FIX levels at or above those found in normal human plasma.

In September 2020, we presented data that showed the persistence of *in vivo* CRISPR/Cas9 edits in regenerated liver tissue, both knockout and insertion, and corresponding durability of effect following a partial hepatectomy ("PHx") and liver regrowth in a murine model. Unlike traditional gene therapy, for which a significant loss (over 80%) in transgene expression was observed in the insertion PHx model, our targeted gene insertion approach yielded durable edits, with no significant loss in expression.

We are further investigating delivery strategies that target tissues outside of the liver. For example, at the Keystone eSymposium: Precision Engineering of the Genome, Epigenome and Transcriptome in March 2021, we presented preclinical data establishing proof-of-concept for non-viral genome editing of bone marrow and HSCs in mice. This represented our first demonstration of systemic *in vivo* genome editing in bone marrow using our proprietary non-viral delivery platform. These results extend our modular *in vivo* capabilities to treat inherited blood disorders such as sickle cell disease.

Ex Vivo *Programs*

We are independently researching and developing proprietary engineered cell therapies to treat various oncological and other disease indications, for example TCR-engineered T cells and chimeric antigen receptor T ("CAR-T") cells for immuno-oncology applications and engineered regulatory T cells for autoimmune disorders. Our diverse product strategy includes multiple elements. In particular:

- We are developing TCR-engineered T cells as immuno-oncological therapies. For example, in our existing collaboration with Ospedale San Raffaele, Milan, a leading European research-university hospital, we have identified optimized TCRs that recognize a tumor target, Wilms' Tumor 1 ("WT1"), that could be used to treat a variety of blood cancers and solid tumors;
- We seek to develop allogeneic cellular therapies, which are those derived from unmatched donors and modified outside of the human body to allow them to be administered to an unrelated patient. These therapies could be used to treat both oncological and immunological diseases; and
- We are also exploring methods to apply CRISPR/Cas9 editing to cluster of differentiation 4 ("CD4") immune cells to induce a non-reverting regulatory T cell phenotype, to create therapies that address autoimmune diseases.

In addition, our partner Novartis is developing therapies directed to selected targets using CAR-T cells for oncology indications, as well as HSC and ocular stem cell ("OSC")-based therapies.

Acute Myeloid Leukemia ("AML") Program

Background

AML includes a heterogenous group of blood cancers arising from the malignant expansion of hematopoietic cells of the myeloid lineage. AML is associated with weakness, fatigue and bleeding resulting from the depletion of healthy myeloid cells, and is typically rapidly progressive and fatal without immediate treatment. AML is an aggressive and hard-to-treat cancer, resulting in less than 30% of patients living more than five years after diagnosis. AML is the most common acute leukemia in adults and is associated with the largest number of annual deaths from leukemia in the U.S. It is estimated that there were over 11,000 deaths due to AML, as well as nearly 20,000 new AML cases in the U.S. in 2020. While AML can occur at any age, the prevalence of the disease increases with age, resulting in a median age at diagnosis of 68 years.

Over the past several years, new treatments have emerged for AML with different mechanisms of action. While these treatments have led to improvements in response rates and in some cases increased overall survival, the outcomes demonstrated thus far have been incremental in nature and long-term outcomes in AML continue to be extremely poor.

NTLA-5001 is our engineered T cell therapy development candidate for the treatment of AML, utilizing our TCR-directed approach to target the WT1 intracellular antigen and restricted to the HLA-A*02:01 allele. As WT1 is overexpressed in >90% of AML blasts, we are developing NTLA-5001 as a broadly applicable treatment for AML, regardless of mutational subtypes of a patient's leukemia. This approach employs CRISPR/Cas9 complexes to knock out and replace the patient's endogenous TCR with a natural, high avidity therapeutic TCR. The resulting cells are engineered to be capable of specific and potent killing of AML blasts without bone marrow cell toxicity. In December 2020, we presented data on NTLA-5001 highlighting the high anti-tumor activity observed in proof-of-concept mouse models of acute leukemias and the faster expansion and superior function of T cells manufactured by our proprietary approach, compared to T cells engineered with a standard genome editing process.

In September 2021, we announced that the FDA has accepted the investigational new drug ("IND") application for NTLA-5001. This first-in-human trial intends to evaluate safety, tolerability, cell kinetics and anti-tumor activity in a single dose of NTLA-5001 in adults who have detectable AML after having received standard first-line therapies. The study will contain a dose escalation and expansion phase, with up to 54 participants. The dose-escalation phase of the study will include two independent arms of up to three cohorts: Arm 1 will consist of adults with AML with lower disease burden, defined as those with less than 5% AML blasts in bone marrow, while Arm 2 will consist of adults with AML with higher disease burden, defined as those greater than or equal to 5% AML blasts in bone marrow. Once a dose is identified in each arm, two expansion cohorts will be opened for further assessment of safety and activity in patients with persistent or recurrent AML who have previously received first-line therapies. We intend to initiate patient screening by year-end in a Phase 1/2a study evaluating NTLA-5001 in adults with persistent or recurrent AML who have previously received first-line therapy. We have also submitted a regulatory application to the U.K.'s MHRA for NTLA-5001.

Ex Vivo *Research Programs*

We are developing engineered cell therapies to treat a range of hematological and solid tumors. We are pursuing modalities, such as TCR, with broad potential in multiple indications. We continue to advance efforts to move from autologous to allogeneic therapies and from liquid to solid tumors. Our researchers are developing and improving cell-engineering manufacturing and delivery processes that, we believe, may allow us to deliver T cell therapies with high levels of editing, robust levels of cell expansion, desirable memory phenotypes, improved function and no translocations above background levels. Our proprietary T cell engineering process enables multiple, sequential gene edits and is a significant improvement over standard engineering processes commonly used to introduce proteins and nucleic acids into cells. These platform advances support NTLA-5001 and other ongoing engineered cell research programs.

At the seventh annual Cold Spring Harbor Laboratory virtual scientific meeting in March 2021, we presented our first preclinical data set on our novel, proprietary cytosine deaminase base editor technology. We demonstrated the technology's potential for enhanced cell engineering, with multiple simultaneous gene knockouts achieving >90% T cell editing efficiency and no detectable increase in translocation above background levels.

In October 2021, at the European Society of Gene and Cell Therapy ("ESGCT") Annual Congress, we shared the first data highlighting our proprietary allogeneic cell engineering platform, demonstrating its potential to prevent immune rejection of allogeneic T cells for application in TCR-T and CAR-T cell therapy. Our proprietary approach leverages a novel combination of sequential gene edits and does not rely on long-term, aggressive immune suppression of patients, or the selective knock out of class I proteins, approaches currently employed by others to address the challenge of host rejection of the adoptive cell therapy. We intend to nominate our first allogeneic cell therapy development candidate by the first half of 2022.

At ESGCT, we also shared new data on our proprietary cell engineering process, demonstrating that LNP-based delivery of CRISPR/Cas9 *ex vivo* allows for sequential editing of T cells with high efficiency, faster expansion and minimal translocations as compared to electroporation. The data support the ability of this platform to be used for a variety of targeting modalities, including CAR and TCRs, and to support both autologous and allogeneic T cell candidates. This LNP-based approach is already being used for NTLA-5001.

Novartis-Led Sickle Cell Disease and Other Research Programs

In December 2019, the research term under our collaboration agreement with Novartis entered into in 2014 (the "2014 Novartis Agreement") ended, although the 2014 Novartis Agreement remains in effect. Under the 2014 Novartis Agreement, Novartis has selected particular CAR-T cell, HSC and OSC targets for continued development. Novartis has initiated clinical studies for OTQ923 and HIX763, two therapeutic candidates, based on CRISPR/Cas9 editing of HSCs, that resulted from our research collaboration with them. Novartis is currently recruiting patients for its Phase 1/2 study of these investigational candidates for treatment of sickle cell diseases. Novartis is developing several other product candidates arising from the 2014 Novartis Agreement. For more information regarding our collaboration with Novartis, see the section below entitled **"Collaborations - *Novartis".***

Collaborations

To accelerate the development and commercialization of CRISPR/Cas9-based products in multiple therapeutic areas, we have formed, and may seek other opportunities to form, strategic alliances with collaborators who can augment our leadership in CRISPR/Cas9 therapeutic development.

Regeneron

As described in Note 7, "Collaborations—Regeneron Pharmaceuticals, Inc.," to our condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q, in April 2016 we entered into a license and collaboration agreement with Regeneron (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 parties will engage in research and development activities aimed at discovering and developing novel technologies and improvements to CRISPR/Cas technology to enhance our genome editing platform. Under the 2016 Regeneron Agreement, we also may access the Regeneron Genetics Center and proprietary mouse models to be provided by Regeneron for a limited number of our liver programs.

On May 30, 2020, we entered into amendment no. 1 (the "2020 Regeneron Amendment") to the 2016 Regeneron Agreement, pursuant to which we expanded the existing collaboration to co-develop potential products for the treatment of hemophilia A and hemophilia B (the "Hemophilia Co/Co"). The collaboration expansion builds upon the jointly developed targeted transgene insertion capabilities designed to durably restore a missing therapeutic protein, and to overcome the limitations of traditional gene therapy. The collaboration was extended until April 2024, at which point Regeneron has an option to renew for an additional two years. The 2020 Regeneron Amendment also grants 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.

Through September 30, 2021, excluding the amounts allocated to Regeneron's purchase of our common stock, we have recorded $145.0 million in upfront payments under the 2016 Regeneron Agreement and the 2020 Regeneron Amendment (the "Amended Agreements") and $36.6 million for research and development services, primarily under the ATTR Co/Co agreement, as described in Note 7 to our condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q. Through September 30, 2021, we have recognized $141.9 million of collaboration revenue under all arrangements, including $6.7 million and $18.7 million during the three and nine months ended September 30, 2021, respectively, and $22.2 million and $46.4 million during the three and nine months ended September 30, 2020, respectively, in the condensed consolidated statements of operations and comprehensive loss. This includes $2.1 million and $3.9 million during the three and nine months ended September 30, 2021, respectively, and $1.2 million and $9.8 million during the three and nine months ended September 30, 2020, respectively, primarily representing payments due from Regeneron pursuant to the ATTR Co/Co agreement, which is accounted for under Accounting Standards Codification 808, *Collaborative Arrangements* ("ASC 808"). These revenues are offset in part by contra-revenue related to the Hemophilia Co/Co agreement amounting to $1.1 million and $2.1 million during the three and nine months ended September 30, 2021, respectively. As of September 30, 2021 and December 31, 2020, we had accounts receivable of $2.1 million related to these arrangements. We had deferred revenue of $57.1 million and $73.9 million as of September 30, 2021 and December 31, 2020, respectively, related to these arrangements.

Novartis

As described in Note 7, "Collaborations—Novartis Institutes for BioMedical Research, Inc.," to our condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q, in December 2014, we entered into a strategic

collaboration agreement with Novartis (the "2014 Novartis Agreement"), primarily focused on the development of new *ex vivo* CRISPR/Cas9-edited therapies using CAR-T cells and HSCs. The agreement was amended in December 2018 (the "Novartis Amendment") to also include research on OSCs.

In December 2019, per the terms of the 2014 Novartis Agreement, the research term ended, although the 2014 Novartis Agreement remains in effect, for which we will be eligible to receive milestone and royalty payments in the future. In June 2021, we entered into Amendment No. 3 (the "Amendment") to the 2014 Novartis Agreement. The Amendment amends Novartis' rights with respect to all the CAR-T Therapeutic Targets (as defined in the 2014 Novartis Agreement) that Novartis selected under the 2014 Novartis Agreement, including (a) making Novartis' license non-exclusive for such CAR-T Therapeutic Targets, (b) removing Novartis' diligence and related reporting obligations for such CAR-T Therapeutic Targets, and (c) refining the scope of Novartis' sublicense rights for such CAR-T Therapeutic Targets. We made a one-time payment to Novartis of $10.0 million within 30 days after the effective date of the Amendment, which was recorded as research and development expense in the condensed consolidated statements of operations and comprehensive loss for the three and nine months ended September 30, 2021. Since December 31, 2020, there have been no other material changes to the key terms of the 2014 Novartis Agreement and the Novartis Amendment. For further information on the terms and conditions of these agreements, please see the notes to the consolidated financial statements included in our Annual Report for the year ended December 31, 2020.

Revenue Recognition – Milestone. In March 2020, the FDA accepted the IND application submitted by Novartis for a CRISPR/Cas9-based engineered cell therapy for the treatment of sickle cell disease. As a result of meeting this milestone, we recognized $5.0 million as collaboration revenue within the condensed consolidated statement of operations and comprehensive loss. In September 2021, an additional milestone was reached and, as a result, we recognized $0.3 million as collaboration revenue within the condensed consolidated statement of operations and comprehensive loss. No other milestones under the 2014 Novartis Agreement and the Novartis Amendment were achieved during the three or nine months ended September 30, 2021 or 2020. We are eligible to receive additional downstream success-based milestones and royalties.

As of September 30, 2021, we had a $0.3 million account receivable related to the milestone noted above and no deferred revenue related to the 2014 Novartis Agreement and the Novartis Amendment. As of December 31, 2020, we had no accounts receivable or deferred revenue related to the 2014 Novartis Agreement and the Novartis Amendment.

License and Collaboration Agreement with New CAR T-Cell Therapy Company

On July 30, 2021, we finalized a transaction in which we, Cellex Cell Professionals GmbH ("Cellex") and funds managed by Blackstone Life Sciences Advisors L.L.C. ("BXLS") established a new universal CAR-T cell therapy company ("NewCo"). On July 30, 2021, we entered into two agreements with NewCo: 1) a license and collaboration agreement (the "LCA"), under which we will collaborate to develop allogeneic universal CAR-T cell therapies and granted NewCo 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 2) a co-development and co-funding agreement (the "NewCo Co/Co") under which we will co-develop and co-commercialize allogeneic universal CAR-T cell products for an immuno-oncology indication. We recognized $0.1 million in revenue related to the LCA, after intra-entity profit elimination, and $0.2 million related to the NewCo Co/Co agreement during the third quarter of 2021. See Note 7 "Collaborations—License and Collaboration Agreement with New CAR-T Cell Therapy Company ("NewCo") for more information.

SparingVision SAS

In October 2021, we and SparingVision SAS ("SparingVision"), a genomic medicine company developing vision saving treatments for ocular diseases, announced a strategic collaboration to develop novel genomic medicines utilizing CRISPR/Cas9 technology for the treatment of ocular diseases. We will grant SparingVision exclusive rights to our proprietary *in vivo* CRISPR/Cas9-based genome editing technology for up to three ocular targets addressing diseases with significant unmet medical need. SparingVision will lead and fund the preclinical and clinical development for the genome editing product candidates pursued under the collaboration. In addition, the parties will research and develop novel self-inactivating adeno-associated virus ("AAV") vectors and LNP-based approaches to address delivery of CRISPR/Cas9 genome editing reagents to the retina. We will receive a 10% equity ownership stake in SparingVision. We will also be eligible to receive certain development and commercial milestone payments (up to approximately $200 million per product) as well as royalties on potential future sales of products arising from the collaboration. We will have an option to obtain exclusive U.S. commercialization rights for product candidates arising from two of three collaboration targets. For product candidates we choose to option, we will pay an opt-in fee, reimburse certain costs, share in 50% of development costs and pay royalties to SparingVision on U.S. sales.

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 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, 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, 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.

Interest Income

Interest income is income earned on our cash, cash equivalents, restricted cash equivalents and marketable securities.

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, 2021 and 2020

The following table summarizes our results of operations for the three months ended September 30, 2021 and 2020:

	Three Months Ended September 30,		Period-to-Period Change
	2021	2020	
	(In thousands)		
Collaboration revenue	$ 7,204	$ 22,220	$ (15,016)
Operating expenses:			
Research and development	60,486	39,756	20,730
General and administrative	18,711	10,566	8,145
Total operating expenses	79,197	50,322	28,875
Operating loss	(71,993)	(28,102)	(43,891)
Interest income	349	262	87
Net loss	$ (71,644)	$ (27,840)	$ (43,804)

Collaboration Revenue

Collaboration revenue decreased by $15.0 million to $7.2 million during the three months ended September 30, 2021, as compared to $22.2 million during the three months ended September 30, 2020. The decrease in collaboration revenue during the three months ended September 30, 2021 is primarily due to $15.3 million related to the transfer of control of the license to develop the Factor VIII target for hemophilia A that was recorded in 2020. 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 approximately $20.7 million to $60.5 million during the three months ended September 30, 2021, as compared to $39.8 million during the three months ended September 30, 2020.

The following table summarizes our research and development expenses for the three months ended September 30, 2021 and 2020, together with the changes in those items in dollars (in thousands) and the respective percentages of change:

	Three Months Ended September 30,		Period-to-Period Change	Percent Change
	2021	2020		
External development expenses by program:				
NTLA-2001	$ 6,767	$ 5,024	$ 1,743	35 %
NTLA-2002	1,280	1,201	79	7 %
NTLA-5001	6,069	3,743	2,326	62 %
Unallocated research and development expenses:				
Employee-related expenses	17,625	10,968	6,657	61 %
Research materials and contracted services	11,919	11,306	613	5 %
Facility-related expenses	7,141	4,712	2,429	52 %
Stock-based compensation	9,017	2,775	6,242	225 %
Other	668	27	641	2374 %
Total research and development expenses	$ 60,486	$ 39,756	$ 20,730	52 %

The increase in research and development expenses for the three months ended September 30, 2021 compared to the three months ended September 30, 2020 was primarily attributable to:

- a $1.7 million increase in external costs related to the development of NTLA-2001, our lead product candidate, primarily due to increased clinical program costs that were incurred during the period;
- a $0.1 million increase in external costs related to the development of NTLA-2002, primarily due to an increase in components as we prepare to enroll patients;
- a $2.3 million increase in external costs related to the development of NTLA-5001, primarily due to an increase in contracted services as we prepare to enter into the clinic;
- a $6.7 million increase in employee-related expenses driven by the expansion of our development organization;
- a $0.6 million increase in research materials and contracted services;
- a $2.4 million increase in facility-related expenses primarily related to rent, depreciation and technology expense allocated to research and development; and
- a $6.2 million increase in stock-based compensation driven by our larger workforce and higher stock prices.

General and Administrative

General and administrative expenses increased by $8.1 million to $18.7 million during the three months ended September 30, 2021, compared to $10.6 million during the three months ended September 30, 2020. This increase was primarily related to employee-related expenses, including stock-based compensation of $3.8 million, driven by our larger workforce and higher stock prices.

Interest Income

Interest income increased by $0.1 million to approximately $0.4 million during the three months ended September 30, 2021 as compared to $0.3 million during the three months ended September 30, 2020. This increase was due to an increase in our overall marketable securities balance as compared to the prior year.

Comparison of Nine Months Ended September 30, 2021 and 2020

The following table summarizes our results of operations for the nine months ended September 30, 2021 and 2020:

	Nine Months Ended September 30,		Period-to-Period Change
	2021	2020	
	(In thousands)		
Collaboration revenue	$ 20,199	$ 51,399	$ (31,200)
Operating expenses:			
Research and development	158,646	112,177	46,469
General and administrative	48,988	33,406	15,582
Total operating expenses	207,634	145,583	62,051
Operating loss	(187,435)	(94,184)	(93,251)
Interest income	780	2,145	(1,365)
Net loss	$ (186,655)	$ (92,039)	$ (94,616)

Collaboration Revenue

Collaboration revenue decreased by $31.2 million to $20.2 million during the nine months ended September 30, 2021, as compared to $51.4 million during the nine months ended September 30, 2020. The decrease in collaboration revenue during the nine months ended September 30, 2021 is primarily due to our recording $15.3 million related to the transfer of control of the license to develop the Factor VIII target for hemophilia A, an $8.4 million one-time cumulative catch-up adjustment related to the modification of the 2016 Regeneron Agreement, and a $5.0 million milestone payment earned from Novartis for the IND submission of OTQ923, all of which were recorded in the first nine months of 2020. 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 $46.5 million to $158.6 million during the nine months ended September 30, 2021, as compared to $112.2 million during the nine months ended September 30, 2020.

The following table summarizes our research and development expenses for the nine months ended September 30, 2021 and 2020, together with the changes in those items in dollars (in thousands) and the respective percentages of change:

	Nine Months Ended September 30,		Period-to-Period Change	Percent Change
	2021	2020		
External development expenses by program:				
NTLA-2001	$ 13,369	$ 17,383	$ (4,014)	-23%
NTLA-2002	4,996	3,490	1,506	43%
NTLA-5001	15,321	8,816	6,505	74%
Unallocated research and development expenses:				
Employee-related expenses	46,927	31,932	14,995	47%
Research materials and contracted services	37,575	27,479	10,096	37%
Facility-related expenses	19,101	14,539	4,562	31%
Stock-based compensation	18,643	7,325	11,318	155%
Other	2,714	1,213	1,501	124%
Total research and development expenses	$ 158,646	$ 112,177	$ 46,469	41%

The increase in research and development expenses for the nine months ended September 30, 2021 compared to the nine months ended September 30, 2020 was primarily attributable to:

- a $4.0 million decrease in external costs related to the development of NTLA-2001, our lead product candidate, primarily due to a decrease in contracted services and manufactured components incurred as compared to the prior period;

- a $1.5 million increase in external costs related to the development of NTLA-2002, primarily due to an increase in component costs as we prepare to enroll patients;
- a $6.5 million increase in external costs related to the development of NTLA-5001, primarily due to an increase in contracted services as we prepare to enter into the clinic;
- a $15.0 million increase in employee-related expenses driven by the expansion of our development organization;
- a $10.1 million increase in research materials and contracted services primarily due to a $10.0 million one-time payment related to the amendment of the 2014 Novartis Agreement;
- a $4.6 million increase in facility-related expenses primarily related to rent, depreciation and technology expense allocated to research and development; and
- an $11.3 million increase in stock-based compensation driven by our larger workforce and higher stock prices.

Through 2021, we expect research and development expenses to increase as we continue to grow our development team, execute clinical trials for ATTR amyloidosis and progress additional programs into the clinic.

General and Administrative

General and administrative expenses increased by $15.6 million to $49.0 million during the nine months ended September 30, 2021, compared to $33.4 million during the nine months ended September 30, 2020. This increase was primarily related to an increase in employee related expenses, including stock-based compensation of $6.8 million, driven by our larger workforce and higher stock prices.

Interest Income

Interest income decreased by approximately $1.4 million to $0.8 million during the nine months ended September 30, 2021 as compared to $2.1 million during the nine months ended September 30, 2020. This decrease was due to a decline in investment income due to overall market conditions.

Liquidity and Capital Resources

Since our inception through September 30, 2021, we have raised an aggregate of approximately $1,815.7 million to fund our operations, of which $276.8 million was through our collaboration agreements, $170.5 million was from our initial public offering and concurrent private placements, $1,086.9 million was from follow-on public offerings, $196.5 million was from at-the-market offerings and $85.0 million was from the sale of convertible preferred stock.

As of September 30, 2021, we had $1,148.7 million in cash, cash equivalents and marketable securities.

In July 2021, we closed an underwritten public offering of 4,758,620 shares of common stock, including the exercise in full of the underwriters' option to purchase an additional 620,689 shares of common stock, at the public offering price of $145.00 per share, for aggregate net proceeds of $648.3 million, after deducting approximately $41.7 million in underwriting discounts and offering costs.

We are eligible to earn a significant amount of milestone payments and royalties, in each case, on a per-product basis under our collaboration with Novartis and on a per-target basis under our collaboration with Regeneron. 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

In August 2019, we entered into an Open Market Sale Agreement (the "2019 Sales 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 $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 Sales Agreement.

During the first half of 2021, we issued 641,709 shares of our common stock in a series of sales at an average price of $72.79 per share in accordance with the 2019 Sales Agreement, for aggregate net proceeds of $45.3 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, 2021, $47.4 million in shares of our common stock remain eligible for sale under the 2019 Sales Agreement.

Funding Requirements

Our primary uses of capital are, and we expect will continue to be, research and development contracted services, compensation and related expenses, laboratory and office facilities, research supplies, legal and regulatory expenses, patent prosecution filing and maintenance costs for our licensed IP and general overhead costs. During 2021, 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 and advance additional programs into clinical development.

Because our lead programs are still in the preclinical or early 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 finance our ongoing cash needs through equity financings and collaboration arrangements. We receive cost reimbursements from Regeneron for the ATTR amyloidosis and hemophilia programs. Additionally, we are eligible to earn milestone payments and royalties, in each case, on a per-product basis under our collaboration with Novartis and on a per-target basis under our collaboration with Regeneron, 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, 2021 will enable us to fund our ongoing operating expenses and capital expenditure requirements beyond the next twenty-four months, excluding any potential milestone payments or extension fees that could be earned and distributed under the collaboration agreements with Regeneron and Novartis 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, 2021 and 2020:

	Nine Months Ended September 30,	
	2021	2020
	(In millions)	
Net cash used in operating activities	$ (170.4)	$ (9.7)
Net cash used in investing activities	(391.7)	(3.6)
Net cash provided by financing activities	734.4	137.7

Net cash used in operating activities

Net cash used in operating activities of $170.4 million during the nine months ended September 30, 2021 primarily reflects the increased spend in our research and development activities, offset in part by the receipt of $4.2 million in payments from our collaboration partners during that period. Net cash used in operating activities of $9.7 million during the nine months ended September 30, 2020 primarily reflects the increased spend in our research and development activities, offset in part by the receipt of a $70.0 million up-front payment and $12.2 million in additional payments under our collaboration with Regeneron and $6.0 million in payments from Novartis.

Net cash used in investing activities

During the nine months ended September 30, 2021 and 2020, our investing activities used net cash of $391.7 million and $3.6 million, respectively. The increase in the nine months ended September 30, 2021 is primarily due to the use of $9.9 million in cash for the purchase of property and equipment and a decrease in marketable securities activity during the period, as $772.8 million in marketable securities were purchased and $391.0 million in marketable securities matured. The decrease in the nine months ended September 30, 2020 is primarily due to the use of $2.6 million in cash for the purchase of property and equipment and a decrease of $1.0 million from marketable securities activity during the period, as $243.8 million in marketable securities matured and $244.8 million in marketable securities were purchased.

Net cash provided by financing activities

Net cash provided by financing activities of $734.4 million during the nine months ended September 30, 2021 includes $648.3 million in net proceeds from a follow-on offering of our common stock, $45.3 million in net proceeds from at-the-market offerings, $39.9 million in cash received from the exercise of stock options and $1.0 million in cash received from the issuance of shares through our employee stock purchase plan. Net cash provided by financing activities of $137.7 million during the nine months ended September 30, 2020 includes $107.7 million in net proceeds from a follow-on offering, $14.7 million in net proceeds from at-the-market offerings, $12.6 million in proceeds from the issuance of common stock to Regeneron in a private placement, $2.0 million in cash received from the exercise of stock options and $0.7 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 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, 2020.

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 nine months ended September 30, 2021. 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, 2020.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements as defined under the rules and regulations of the SEC.

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, 2021, we had cash equivalents, restricted cash equivalents and marketable securities of $1,149.9 million consisting of interest-bearing money market accounts, commercial paper, asset-backed securities, corporate and financial institution debt securities, and U.S. Treasury and other government 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, 2021.

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, 2021.

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 nine months ended September 30, 2021 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. 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 for the year ended December 31, 2020 and in other documents that we file with the SEC, in evaluating us and our business. 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 it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations.

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 product candidates, 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 clinical study of NTLA-2001, 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.
- Business interruptions resulting from the coronavirus disease 2019 ("COVID-19") outbreak or similar public health crises could cause a disruption of the development of our product candidates and adversely impact our business.
- 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 with Novartis Institutes for BioMedical Research Inc. ("Novartis") and Regeneron Pharmaceuticals, Inc. ("Regeneron"), and if either of these collaboration agreements were to be terminated or materially altered in an adverse manner, our business, financial condition, results of operations and prospects would 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. The outcome of on-going 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 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 beginning to clinically test our *in vivo*, and have recently obtained authorization to start clinical testing of one of our *ex vivo* product candidates and have not obtained clearance to start clinical testing of our engineered product candidates, NTLA-5001. Further, we are unaware of any

clinical trials validating safety and efficacy having been completed by any third parties. 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 on-going 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 therapeutic product will translate to other CRISPR/Cas9 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, health care 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, health care 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 early 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 early 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.

Because these are new therapeutic approaches, discovering, developing, manufacturing and commercializing our product candidates 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 commence clinical trials in the U.S. from the FDA through an investigational new drug application ("IND") or from other regulatory agencies outside the U.S., such as the U.K.'s Medicines and Healthcare products Regulatory Agency ("MHRA") or the New Zealand Medicines and Medical Devices Safety Authority ("MEDSAFE"), 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 therapeutics, which may require additional significant testing or data compared to more traditional therapies;
- successfully developing processes for the safe administration of these products, 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 or modify the design of our clinical trials or perform more extensive or lengthier clinical testing compared to existing therapeutic modalities;
- 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, 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 requiring amendments to our regulatory filings, before permitting us to initiate or rely on a clinical trial;
- we may be unable to develop a manufacturing process and distribution network with a cost of goods that allows for an attractive return on investment;
- 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 approving our product candidates, or their interpretation of the approval requirements may not be what we anticipate; and
- we may not ultimately obtain regulatory approval for a BLA, or corresponding applications outside the U.S., such as a Marketing Authorization Application ("MAA") from the U.K. and other similar regulatory authorities, such as the European Medicines Agency ("EMA"), which may have very limited or no experience with the clinical development of CRISPR/Cas9 therapeutics.

In addition, disruptions caused by the evolving COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our ongoing and planned clinical trials. We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted or the relevant ethics committee, the Data Safety Monitoring Board ("DSMB") for such trial, or the FDA or other relevant regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or 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;
- 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 or insertion of a sequence into certain locations in a patient's chromosome, could lead to cancer, other aberrantly functioning cells or other diseases, including death;
- transient expression of the Cas9 protein 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, clinical trials using engineered cell-based gene therapies may require unique products to be created for each patient and such individualistic manufacturing may be both inefficient and cost-prohibitive.

To date, human clinical trials utilizing either *in vivo* or *ex vivo* CRISPR/Cas9-based therapeutics, including our clinical trial for NTLA-2001 for transthyretin ("ATTR") amyloidosis, are still at an early stage. 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. 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 that would potentially harm our business.

We received IND authorization from the FDA for NTLA-5001 in September 2021 and expect to initiate patient screening in a Phase 1/2a clinical trial by year-end of 2021. In addition, we received authorization in October 2021 from the U.K.'s MHRA and New Zealand's MEDSAFE to initiate a Phase 1/2 study evaluating NTLA-2002 for the treatment of adults with hereditary angioedema ("HAE"), which we expect to initiate enrollment in by year-end of 2021. We may experience manufacturing delays or other issues that prevent us from executing the first-in-human clinical trials for NTLA-5001 or NTLA-2002 on the timelines we expect. Moreover, we cannot guarantee that FDA, 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 NTLA-5001.

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 create 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 focus are on the development of therapies using CRISPR/Cas9 gene-editing technology. Genome editing companies focused on CRISPR based technologies include: Beam Therapeutics Inc., Caribou Biosciences, Inc., CRISPR Therapeutics AG, Editas Medicine, Inc. and ToolGen, Inc.

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

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

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

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 (both autologous and allogeneic) 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 the Industry

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 clinical study of NTLA-2001. 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. As a result, 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 above risk factor section entitled "Risks Related to Preclinical and Clinical Development".

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 future product candidates.

Therapeutic applications of genome editing technologies, and CRISPR/Cas9 in particular, for both *in vivo* products and in engineered cell therapies, 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, 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 future 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 Risk Evaluation and Mitigation Strategy ("REMS") or similar strategy;
- be sued; or
- experience damage to our reputation.

Additionally, our future 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 future 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 for other product candidates being deemed appropriate for clinical development and ultimately approval, including NTLA-2002 for HAE or NTLA-5001 for AML, by a regulatory agency. Even if we are successful in building our pipeline of product candidates, completing clinical development, establishing the necessary manufacturing processes and capabilities, obtaining regulatory approvals and commercializing product candidates will require substantial additional funding and are subject to the risks of failure inherent in therapeutic product development. Investment in biopharmaceutical product development involves significant risk that any potential product candidate will fail to demonstrate acceptable safety and efficacy profiles, gain regulatory approval, or become commercially viable.

We cannot provide any assurance that we will be able to successfully advance any of our product candidates, including NTLA-2001, NTLA-2002 or NTLA-5001, 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 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, health care 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 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 health care 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 health care 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, gene 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 health care 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 gene 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.

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’ coverage decisions. Other jurisdictions have agencies, such as the National Institute for Health and Care Excellence (“NICE”) 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 gene-modifying 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.

Legal, political and economic uncertainty surrounding the exit of the United Kingdom from the EU is a source of instability and uncertainty.

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. Although this agreement is comprehensive and provides some details on how aspects of the U.K. and EU's relationship regarding medicinal products will operate, particularly in relation to Good Manufacturing Practice, it does not cover many areas of regulation pertinent to the biopharmaceutical industry, so many complexities remain. Many of the regulations that now apply in the U.K. following the transition period (including financial laws and regulations, tax, intellectual property rights, data protection laws, supply chain logistics, environmental, health and safety laws and regulations, medicine approval and regulations, immigration laws and employment laws), will likely be amended in future as the U.K. determines its new approach, which may result in significant divergence from EU regulations. This lack of clarity on future U.K. laws and regulations and their interaction with the EU laws and regulations increases our regulatory burden of operating in and doing business with both the U.K. and the EU.

The long-term effects of Brexit will depend in part on how the EU-U.K. TCA, and any future agreements signed by the U.K. and the EU, take effect in practice. Such a withdrawal from the EU is unprecedented, and it is unclear how the restrictions on the U.K.'s access to the European single market for goods, capital, services and labor within the EU and the wider commercial, legal and regulatory environment, could impact our current and future operations and clinical activities in the U.K.

We may also face new regulatory costs and challenges that could have an adverse effect on our operations as a result of Brexit. Since the regulatory framework in the U.K. covering quality, safety and efficacy of medicinal products, clinical trials, marketing authorization, commercial sales and distribution of medicinal products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime with respect to the approval of any of our future product candidates in the U.K., because U.K. legislation has the potential to diverge from EU legislation. For instance, Great Britain is no longer covered by the centralized procedure for obtaining European Economic Area ("EEA")-wide marketing authorizations from the EMA for medicinal products and a separate process for authorization of drug products is required in Great Britain under the Northern Ireland Protocol between the EU and the U.K., where the EU regulatory framework will continue to apply in Northern Ireland and centralized EU authorizations will continue to be recognized in Northern Ireland only. For a period of two years from January 1, 2021, 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 will still be required. 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.

Until there is greater understanding on how the terms of the TCA will take effect in the long-term, and until the terms of other potential agreements that the U.K. may eventually enter into with the EU are known, it is not possible to determine the extent of the impact that the U.K.'s departure from the EU and/or any related matters may have on us; however any of these effects of Brexit, and others we cannot anticipate, could negatively impact our business and results of operations in the U.K. Likewise, similar actions taken by European and other countries in which we operate could have a similar or even more profound impact.

The uncertainty concerning the U.K.'s legal, political and economic relationship with the EU following Brexit may also be a source of instability in the international markets, create significant currency fluctuations, and/or otherwise adversely affect trading agreements or similar cross-border co-operation arrangements (whether economic, tax, fiscal, legal, regulatory or otherwise).

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, as well as data privacy and the relationship with health care providers, are strictly regulated by laws in the US and most other jurisdictions in which we intend to seek approval for our product candidates. 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. In addition, 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.

The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which generally prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or certain rebates) for referring an individual or inducing a transaction for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violators are subject to civil and criminal fines and penalties, as well as imprisonment and exclusion from government healthcare programs;

- federal civil and criminal false claims laws, including the federal False Claims Act ("FCA"), which generally prohibit knowingly making false or fraudulent claims for payment or approval from the federal government, including Medicare, Medicaid and other government payors, or knowingly seeking to conceal, decrease or avoid an obligation to pay money to the federal government. Certain indirect acts, such as promoting products off-label, can be deemed FCA violations by a manufacturer even it did not submit the claim directly to the government payor. Further, under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "Affordable Care Act", or "ACA"), a violation of the federal Anti-Kickback Statute may also constitute a false or fraudulent claim under the FCA. These laws impose criminal and civil penalties on violators. Private individuals may bring civil whistleblower or *qui tam* actions for alleged FCA violations on behalf of the federal government;

- the U.S. federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act," created under the ACA, and their implementing regulations, which require manufacturers of certain products paid under Medicare, Medicaid or the Children's Health Insurance Program, including biopharmaceutical products, to report information related to payments or other consideration made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare providers and teaching hospitals, as well as ownership and investment interests held by these healthcare providers and their immediate family members in the manufacturer. Failure to comply could result in civil monetary penalties. Effective January 1, 2022, the U.S. federal physician transparency reporting requirements will extend to include transfers of value made to certain non-physician providers (physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists & anesthesiologist assistants, and certified nurse-midwives);

- the Foreign Corrupt Practices Act ("FCPA") and other laws, which generally prohibit improper payments or offers of payments to foreign governments and their officials and political parties by U.S. persons and entities to obtain or retain business. In the U.K., for example, the U.K. Bribery Act 2010 prohibits giving financial or other advantages to encourage persons to perform their functions improperly;

- the Federal Food, Drug and Cosmetic Act, which prohibits the commercialization of adulterated or misbranded drugs, and the Public Health Service Act, which prohibits the commercialization of biological products without a biologics license;

- analogous state and foreign legal requirements that:
  - may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and may be broader in scope than their federal equivalents, such as state anti-kickback and false claims laws;
  - require following the pharmaceutical industry's voluntary compliance guidelines and the federal government's relevant compliance guidance, or otherwise restrict payments to healthcare providers;
  - require reporting information related to payments and other consideration to physicians and other healthcare providers or marketing expenditures; and
- other national and local laws that govern the distribution and sale of pharmaceuticals, including imposing requirements regarding licensing, record-keeping, storage and security requirements.

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 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 government, 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., 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 individually identifiable health information 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 became effective in January 2020 and enforceable in July 2020;
- other U.S. states, such as Massachusetts, Nevada, Illinois, Colorado, Virginia, Pennsylvania, Ohio, North Carolina, New Jersey and New York, have enacted and/or are considering laws that impose stringent privacy and/or data security requirements; and

- in the EU and EEA the collection and use of personal data is regulated by the General Data Protection Regulation ("GDPR") and the members' related data protection and privacy laws, and in the U.K. by its Data Protection Act 2018 and, as of January 1, 2021, the U.K. GDPR (such laws collectively being described as "European Data Protection Law"). Because the European Data Protection Law applies to any business that provides goods or services to individuals in the EU or U.K., it could apply to us. The European Data Protection Law imposes strict requirements, including special protections for "sensitive information," which includes health and genetic information of individuals in the EU or the U.K.; expanded disclosures about the personal data use; information retention limitations; mandatory data breach notification requirements; and additional oversight obligations relating to third-parties retained to process the personal data. The 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. It also has strict requirements on the transfer of personal data out of the EU or the U.K. to regions that have not been deemed to offer "adequate" privacy protections, such as the U.S. 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 20,000,000 Euro, 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 the European Data Protection Law, may be onerous and adversely affect our business, financial condition, results of operations and prospects. Further, due to Brexit, we may have additional costs and operational challenges in complying with the U.K. GDPR and any other developments regulation the transfer between the U.K. and EU. 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 health care 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.

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 health care 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 health care 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 health care 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, 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. At this time, the full effect that the Affordable Care Act would have on our business remains unclear.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA and we expect there will be additional challenges and amendments to the ACA in the future. The Tax Cuts and Jobs Act of 2017 ("Tax Act") includes a provision that decreased the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, commonly referred to as the "individual mandate," to $0, effective January 1, 2019. On December 14, 2018, a federal district court in Texas ruled the individual mandate is a critical and inseverable feature of the ACA and, therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional, and remanded the case to the lower court to reconsider its earlier invalidation of the full ACA. Following an appeal by certain defendants, on June 17, 2021, the U.S. Supreme Court dismissed the plaintiffs' challenge to the ACA for lack of standing without specifically ruling on the constitutionality of the ACA, and reversed the Fifth Circuit's judgment and remanded the case with instructions to dismiss. It is unclear how other healthcare reform measures of the Biden administrations or other efforts, if any, to challenge, repeal or replace the ACA, will impact our business.

Other legislative changes relevant to the health care system have been adopted in the U.S. since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013, and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken. However, pursuant to the Coronavirus Aid, Relief and Economic Security Act (the "CARES Act") and subsequent legislation, the Medicare sequester reductions under the Budget Contract Act of 2011 have been suspended from May 1, 2020 through December 31, 2021 due to the COVID-19 pandemic. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers, cancer centers and other treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Additionally, on July 9, 2021, President Biden issued an executive order directing the FDA to, among other things, work with states and tribes to safely import prescription drugs from Canada and to continue to clarify and improve the approval framework for generic drugs and biosimilars, including the standards for interchangeability of biological products, facilitate the development and approval of biosimilar and interchangeable products, clarify existing requirements and procedures related to the review and submission of BLAs, and identify and address any efforts to impede generic drug and biosimilar competition. It is unclear whether the FDA will make changes or additions to current requirements and procedures relating to BLAs and, if so, how such changes or additions could impact our business.

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 health care 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 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 the COVID-19 pandemic; 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 likely will be 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. In addition, we rely on third-party CMOs to manufacture these components and the final product candidates. 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. Even if we decide to manufacture the product candidates or their components ourselves, we may face extremely high costs and long timelines to build and maintain manufacturing facilities. 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, quality-control 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 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, 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 also have 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 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 a significant portion of our workforce working from home for extended periods of time due to the COVID-19 pandemic 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 and other means to affect service reliability and threaten the confidentiality, integrity, and availability of information. 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 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 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 and cloud computing platform providers and Software as a Service 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, 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, Software as a Service vendors or our third-party web hosting providers, and they also may be vulnerable to damage or interruption from natural disasters, cybersecurity attacks, terrorist attacks, power outages 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.

In addition, regulatory agencies in and outside the U.S. may experience delays or backlogs due to the worldwide COVID-19 pandemic.

Social media 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 the Company, 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. 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.

Risks Related to the COVID-19 Pandemic

Business interruptions resulting from the COVID-19 outbreak or similar public health crises could delay or cause a disruption of the development of our product candidates and adversely impact our business.

Public health crises, such as pandemics or similar outbreaks, could adversely impact our business. The current COVID-19 pandemic has continuously evolved, and to date has led to the implementation of various responses, including government-imposed quarantines, travel restrictions and other public health safety measures, as well as reported adverse impacts on healthcare resources, facilities and providers, in Massachusetts, across the U.S. and in other countries. The U.S. government, as well as certain foreign governments, have imposed restrictions on travel to or from the U.S. and other jurisdictions, which may delay or prevent us from conducting our business in a timely and efficient manner. The extent to which COVID-19 impacts our operations or those of our third-party partners will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the outbreak, additional or modified government actions, new information that will emerge concerning the severity and impact of COVID-19 and the actions to contain COVID-19 or address its impact in the short and long term, among others.

Additionally, completion of our clinical trial for NTLA-2001 for ATTR amyloidosis, as well as timely completion of preclinical activities and initiation of planned clinical trials for other product candidates, such as NTLA-2002 for HAE and NTLA-5001 for AML, is dependent upon the availability of, for example, preclinical and clinical trial sites, researchers and investigators, regulatory agency personnel, and materials, which may be adversely affected by global health matters, such as pandemics. We plan to conduct preclinical activities and clinical trials for our investigational drug product candidates in geographies which are currently being affected by COVID-19.

Further, in response to the pandemic and in accordance with direction from state and local government authorities, we have restricted and may continue to restrict access to our facilities mostly to personnel and third parties who must perform critical activities that must be completed on-site, limited the number of such personnel that can be present at our facilities at any one time, and requested that personnel work remotely, as appropriate. In the event that governmental authorities were to further modify current restrictions, our employees conducting research and development or manufacturing activities may not be able to access our laboratory or manufacturing space, and our core activities may be significantly limited or curtailed, possibly for an extended period of time.

Some factors from the COVID-19 pandemic that could delay or otherwise adversely affect the completion of our preclinical activities and our ongoing and planned clinical trials for our investigational drug product candidates, as well as our business generally, include:

- the potential diversion of healthcare resources away from the conduct of preclinical activities and clinical trials to focus on pandemic concerns, including the availability of necessary materials and the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our prospective clinical trials;
- risk that participants enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- risk that we are unable to enroll and retain participants in our clinical trials in adequate numbers;
- limitations on travel that could interrupt key preclinical activities and trial activities, such as limited operations at laboratory facilities, clinical trial site initiations and monitoring, domestic and international travel by employees, contractors or patients to clinical trial sites, including any government-imposed travel restrictions or quarantines that will impact the ability or willingness of patients, employees or contractors to travel to our research, manufacturing and clinical trial sites or secure visas or entry permissions, any of which could delay or adversely impact the conduct or progress of our prospective clinical trials;

- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- interruption or delays in the operations of the FDA, MHRA and comparable foreign regulatory agencies, which may impact review, inspection, authorization and approval timelines;
- interruption in global shipping affecting the transport of clinical trial materials, such as patient samples, investigational drug product candidates and conditioning drugs and other supplies used in our prospective clinical trials;
- interruption of, or delays in receiving, supplies of our investigational drug product from our CMOs due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- limitations on our business operations by local, state, or the federal government that could impact our ability to conduct our preclinical or clinical activities, including completing our IND-enabling studies or our ability to select future development candidates;
- business disruptions caused by potential workplace, laboratory and office closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments and operations, staffing shortages, travel limitations, or communication or mass transit disruptions, any of which could adversely impact our business operations or delay necessary interactions with local regulators, ethics committees, manufacturing sites, research or clinical trial sites and other important agencies and contractors;
- business disruptions or cybersecurity risks associated with a substantial portion of our workforce working from home for extended periods of time; and
- the impact on the valuation of our marketable securities and other financial assets due to market volatility.

These and other factors arising from COVID-19 could worsen in countries that are already afflicted with coronavirus or could continue to spread to additional countries, each of which could further adversely impact our ability to conduct clinical trials and our business generally, and could have a material adverse impact on our operations and financial condition and results.

In addition, the trading prices for our common stock and other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. As a result, we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms. The COVID-19 outbreak continues to rapidly evolve. The extent to which the outbreak may impact our business, preclinical studies and ongoing and planned clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions and other actions to contain the outbreak or address its impact, such as social distancing and quarantines or lock-downs in the U.S. and other countries, business closures or business disruptions and the effectiveness of actions taken in the U.S. and other countries to contain and address the disease.

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 significant resources in developing large scale manufacturing, analytical processes, 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 an early clinical-stage company. We were founded and commenced operations in mid-2014. All of our product candidates are still in the preclinical development or early 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 very early-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 $71.6 million for the three months ended September 30, 2021. As of September 30, 2021, we had an accumulated deficit of $621.8 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. Although we believe that our cash, cash equivalents, and marketable securities will enable us to fund our operating and capital expenditure requirements at least through the next twenty four months, we cannot predict the impact of the COVID-19 pandemic on future results of operations and financial condition due to a variety of factors, including the health of our employees, the ability of suppliers to continue to operate and deliver, the ability of Intellia to maintain operations, continued access to transportation resources, any further government and/or public actions taken in response to the pandemic and ultimately the length of the pandemic. 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. Given the impact of COVID-19 on the U.S. and global financial markets, we may be unable to access further equity or debt financing when needed.

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, such as the COVID-19 pandemic. 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 and, more recently, due to the COVID-19 pandemic 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 impact on the economic and financial markets of the COVID-19 pandemic has depressed the valuation of public companies, which could 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, including those resulting from the current COVID-19 pandemic, 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 (such as the COVID-19 pandemic), 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 (or if the COVID-19 pandemic continues to disrupt or prevent regular inspections, reviews, or other regulatory activities conducted by regulatory agencies) 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 Novartis and Regeneron

Our technological advancements and any potential for revenue may be derived in part from our collaborations with Novartis and Regeneron, and if either of these collaboration agreements were to be terminated or materially altered, our business, financial condition, results of operations and prospects would be harmed.

In December 2014, we entered into a collaboration agreement with Novartis, which we amended in December 2018 and June 2021 (collectively, the "Novartis Agreement") regarding the discovery of new CRISPR/Cas9-based therapies principally using CAR-T cells, hematopoietic stem cells ("HSCs") and certain limbal stem cells selected by Novartis. Under the Novartis Agreement, Novartis committed to advance programs in these cells, and we granted it exclusive rights to further develop and commercialize the product candidates against targets it selected during the research term arising out of the programs. On June 14, 2021, the Novartis Agreement was amended ("Amendment No. 3") with respect to Novartis' rights to all the CAR-T Therapeutic Targets (the "Targets") that Novartis selected, including (a) making Novartis' license non-exclusive for such Targets, (b) removing Novartis' diligence and related reporting obligations for such Targets, and (c) redefining the scope of Novartis' sublicense rights for such Targets. We also agreed to pay to Novartis a one-time payment of $10.0 million within 30 days after the effective date of Amendment No. 3. The research portion of our agreement with Novartis ended in December 2019, and we cannot guarantee that Novartis will continue to pursue any of its selected programs.

In April 2016, we entered into a collaboration agreement with Regeneron, which we amended in May 2020 (the "Amended Regeneron Agreement"). The Amended Regeneron Agreement includes a product component to research, develop and commercialize CRISPR/Cas-based therapeutic products primarily focused on genome editing in the liver, as well as a technology collaboration component, under which we and Regeneron will engage in research and development activities aimed at discovering and developing novel technologies and CRISPR/Cas technology improvements to enhance our genome editing platform. Pursuant to the Amended Regeneron Agreement, we granted Regeneron exclusive rights to select up to 15 initial targets, subject to certain restrictions and modifications. We retained the rights to solely develop certain indications, and have the right to choose additional liver targets for our own development during the collaboration term. Both parties have defined rights to enter into co-development and co-promotion ("Co/Co") agreements for indications selected by the other. Certain indications, such as ATTR amyloidosis, hemophilia A and hemophilia B are subject to Co/Co agreements. For example, in July 2018, we entered into an ATTR Co/Co under which we are the clinical and commercial lead for ATTR amyloidosis products. In December 2019, Regeneron exercised its right under the ATTR Co/Co agreement to modify its share of worldwide development costs and profits from 50% to 25% as of mid-June 2020. In May 2020, we entered into two co-development and co-funding

agreements directed to each of hemophilia A and hemophilia B (the "Hemophilia Co/Co") agreements, under which Regeneron will be the clinical and commercial lead, for these programs. Under the Hemophilia Co/Co agreements, worldwide development costs and profits of any future covered products will be split between Regeneron and us, 65% and 35%, respectively.

Either Novartis or Regeneron may change its strategic focus or pursue alternative technologies in a manner that results in reduced, delayed or no revenue to us. Each of Novartis and Regeneron has a variety of marketed products and product candidates either by itself or with other companies, including some of our competitors, and the respective corporate objectives of Novartis or Regeneron may not be consistent with our best interests. Regeneron may change its position regarding its participation and funding of our joint ATTR amyloidosis activities, which may impact our ability to successfully pursue that program. If either of our collaboration partners fails to develop, obtain regulatory approval for or ultimately commercialize any product candidate from the development programs governed by the respective collaboration 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 of the collaboration agreements, or dispute or litigation proceedings we may have with either Novartis or Regeneron 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.

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 discovery and 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 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 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. 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 the New Company

We launched a new company 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 a new company ("NewCo") alongside Cellex Cell Professionals GmbH ("Cellex") and Blackstone Life Sciences Advisors L.L.C. ("BXLS") (the "NewCo Launch"). NewCo acquired GEMoaB GmbH ("GEMoaB"), a wholly-owned subsidiary of Cellex. NewCo combines GEMoaB's clinical-stage universal CAR-T program and platforms with our allogeneic universal cell engineering platform. In connection with the NewCo Launch, we entered into a license and collaboration agreement with NewCo (the "NewCo License"), under which we will collaborate to develop allogeneic universal CAR-T cell therapies, as well as a co-development and co-funding agreement (the "NewCo Co/Co Agreement") to develop allogeneic universal CAR-T cell products targeted to a particular undisclosed immuno-oncology therapeutic target. NewCo may not be successful in the timeframe we expect, or at all. In addition, if NewCo fails to develop, obtain regulatory approval for or ultimately commercialize any product candidate from its development programs, including those governed by the respective NewCo License or NewCo Co/Co Agreement, or breaches or terminates such agreements, our business, financial condition, results of operations and prospects could be harmed.

Additionally, we, BXLS, and Cellex (and certain related entities) each have equal ownership of NewCo and therefore share control over portions of the operations of NewCo. Because of our minority ownership in NewCo, we have a lesser degree of

control over its business operations, 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 NewCo who may have business interests, strategies or goals that are inconsistent with ours. These risks include the possibility that NewCo, 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 NewCo, we may be required to include NewCo's financial information in our condensed consolidated financial results. We have not previously included a minority-owned subsidiary in our financial statements and therefore are subject to increased risk in accurately representing and incorporating NewCo'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 do not currently own any facility that may be used as our clinical-scale manufacturing and processing facility 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, potent, pure or effective.

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. 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 they cannot successfully manufacture material that conforms to our specifications and the strict relevant regulatory requirements, our CMOs will not be able to secure or maintain regulatory approval for their 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 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 products or product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from 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 manufacturing 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. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our product candidates. 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.

Events such as the ongoing COVID-19 pandemic could adversely impact the ability of our vendors, including CMOs, to manufacture supplies, process and deliver our product candidates, or to otherwise meet our requirements or those of the applicable regulatory agencies. For example, since the beginning of the COVID-19 pandemic, three vaccines for COVID-19 have been granted Emergency Use Authorization by the FDA, and one of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing capacity for the products needed for our clinical trials, which could lead to delays in these trials. Additionally, these events could also impact the regulatory agencies' ability to inspect and approve our vendors, including CMOs, within our currently expected timeframe.

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.

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 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. In addition, the COVID-19 pandemic or similar events, and responsive governmental actions, could divert healthcare resources, including necessary materials and clinical trial personnel, away from our clinical trial

sites to focus on pandemic concerns. 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 a similar event) 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, including the areas of technology research, product development and manufacturing, clinical, regulatory and quality affairs and, 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, Glenn Goddard, our Executive Vice President and Chief Financial Officer, David Lebwohl, our Executive Vice President and Chief Medical Officer, James Basta, our Executive Vice President, General Counsel and Corporate Secretary, 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. Finally, events such as the COVID-19 pandemic and government restrictions and directives,

including immigration policy changes, could adversely impact our ability to recruit, retain or replace key employees necessary to achieve our objectives and strategic imperatives, 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 specific guidance and 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 products. 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 ("ICTRP"). 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). Further, a clinical trial may be suspended or terminated by us, the relevant IRBs or ethics committees the trial's DSMB, or the FDA or other regulatory authorities 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.

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 IV 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.

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 national, 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.

Given that we are conducting a clinical trial in the U.K., and our current and future requests for approval to conduct clinical trials in the U.K. and other jurisdictions outside the U.S., we are and may be subject to additional privacy laws. For example, the GDPR applies extraterritorially, and we may be subject to the GDPR because of data processing activities that involve the personal data of individuals in the EU or the U.K. in connection with EU or U.K. clinical trials. As discussed above, the GDPR regulates the processing of personal data of data subjects in the EU or the U.K. by imposing a broad range of strict requirements on companies subject to the GDPR, including requirements relating to having legal bases for processing personal data and transferring such information outside the EU or the U.K., including to the U.S., providing robust disclosures to individuals regarding the processing of their personal data, keeping personal data secure, having data processing agreements with third parties who process personal data, responding to individuals' requests to exercise their rights in respect of their personal data, reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments, and record-keeping. In the event of non-compliance with the GDPR, 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. We face uncertainty as to the exact interpretation of the new requirements and we may be unsuccessful in implementing all measures required by data protection authorities or courts in interpretation of the law.

In addition, as it relates to processing and transfer of health and genetic data, the GDPR specifically allows national laws to impose additional and more specific requirements or restrictions, and European laws have historically differed quite substantially in this field, leading to additional uncertainty.

If we are investigated by a European data protection authority, we may face fines and other penalties. Any such investigation or charges by European data protection authorities could have a negative effect on our existing business and on our ability to attract and retain new clients or pharmaceutical partners. We may also experience hesitancy, reluctance, or refusal by European or multi-national clients or pharmaceutical partners to continue to use our products and solutions due to the potential risk exposure as a result of the current (and, in particular, future) data protection obligations imposed on them by certain data protection authorities in interpretation of current law, including the GDPR. Such clients or pharmaceutical partners may also view any alternative approaches to compliance as being too costly, too burdensome, too legally uncertain, or otherwise objectionable and therefore

decide not to do business with us. Any of the foregoing could materially harm our business, prospects, financial condition and results of operations.

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 wastes. 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 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. This law 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 mRNA encoding Cas9 protein, guide RNAs, 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 upon 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.

Similarly, on October 17, 2018, we initiated an arbitration proceeding with JAMS against Caribou asserting that Caribou violated the terms and conditions of the Caribou License, as well as other contractual and legal rights, by using and seeking to license to third parties technology covered by two patent families (described in, for instance, PCT No. PCT/US2016/015145 and PCT No. PCT/US2016/064860, and related patents and applications) relating to specific structural or chemical modifications of guide RNAs, that were purportedly invented or controlled by Caribou, in our exclusive human therapeutic field. Caribou asserted that the two families of IP are outside our exclusive license rights under the Caribou License.

On September 26, 2019, we announced that the arbitration panel issued an interim award concluding that both the structural and chemical guide RNAs modification technologies were exclusively licensed to us by Caribou under the Caribou License. After concluding that the chemical modification technology was within the scope of our exclusive license from Caribou, the arbitration panel nevertheless noted that its decision could delay or otherwise adversely impact the development of these modified guide RNAs as human therapeutics. It also noted that we currently are not using these modified guide RNAs in any of our active programs. Thus, solely with respect to the particular modified guide RNAs, the arbitration panel stated that it will declare that Caribou has an equitable "leaseback," which it described as exclusive, perpetual and worldwide.

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. On August 26, 2019, the PTAB redeclared the interference to include additional UC/Vienna/Charpentier patent applications covering the invention that had also been found allowable by the USPTO. On September 10, 2020, the PTAB issued an order that, among other matters, advanced the proceeding to the priority phase, where both UC/Vienna/Charpentier, which will have the burden of proof, and the Broad Institute will present their respective evidence seeking to prove that they, invented first. As of September 30, 2021, the interference involves 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 December 14, 2020, the PTAB declared an additional interference between the same 14 allowable patent applications in the UC/Vienna/Charpentier portfolio, and one patent application owned by ToolGen, Inc. And, on June 21, 2021, the PTAB declared another interference between the same UC/Vienna/Charpentier 14 allowable patent applications 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. These two latter interferences are still in their motion phases where the PTAB may consider, among other matters, which party will have the burden of proof in their respective priority phases. If either the Broad, 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 UC/Vienna/Charpentier application was filed 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 UC/Vienna/Charpentier application, 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, we may be required to pay milestones and royalties based on our revenues, including sales revenues of our products, utilizing the technologies licensed or sublicensed from third parties, including Caribou, Novartis, Regeneron and OSR, 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 license rights under these license agreements, we will need to meet certain specified milestones, subject to certain cure provisions, in the development of our product candidates. Further, our licensors (or their licensors) or licensees may dispute the terms, including amounts, that we are required to pay under the respective license agreements. If these claims were to result in a material increase in the amounts that we are required to pay to our licensors, or in a claim of breach of the license, 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. Delay or failure by these third parties could adversely affect the continuation of our license agreements with their third-party 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 guide RNA molecules, as well as methods of editing DNA *in vitro* or *ex vivo* using Cas9 and single guide RNAs. 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 guide RNA ("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 national 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.

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 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.

In addition, the trading prices for our common stock and other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. The extent to which the outbreak may impact our business, preclinical studies and ongoing and planned clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the emergence of new variants of the disease, the ability of governments to vaccinate their populations and that existing vaccines can treat any new variants effectively, the ultimate containment of the disease, the modification or lifting of travel restrictions and other actions implemented to contain the outbreak or address its impact, such as social distancing and quarantines or lock-downs in the U.S. and other countries, business closures or business disruptions, and the ultimate effectiveness of other actions taken in the U.S. and other countries to contain and address the disease. A resurgence or other negative developments relating to the pandemic may require us to again restrict access to our offices and laboratories, or to pause or suspend preclinical research and our clinical trial; and, further, may disrupt our manufacturing and supply chain or those of our third-party suppliers and manufacturers.

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, 2021, our executive officers, directors, 5% or greater stockholders and their affiliates beneficially owned approximately 35.2% 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.

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.

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 in November 2017, June 2020, December 2020, and July 2021. 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.

On August 23, 2019, we filed a Registration Statement on Form S-3, as amended (the "2019 Shelf") with the SEC, which was declared effective on September 12, 2019 (File No. 333-233448) in relation to the registration of common stock, preferred stock, debt securities, warrants and units of any combination thereof. We also simultaneously entered into an Open Market Sale Agreement (the "2019 Sales Agreement") with the Sales Agent, to provide for the offering, issuance and sale of up to an aggregate amount of $150.0 million of our common stock from time to time in "at-the-market" offerings under the 2019 Shelf and subject to the limitations thereof. We will pay to the Sales Agent cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2019 Sales Agreement. In December 2019, we issued 287,231 shares of our common stock at an average price of $16.48 per share in accordance with the 2019 Sales Agreement for aggregate net proceeds of $4.4 million, after payment of cash commissions to the Sales Agent and approximately $0.2 million related to legal, accounting and other fees in connection with the sales. During the year ended December 31, 2020, we issued 2,270,161 shares of our common stock in a series of sales at an average price of $22.53 per share in accordance with the 2019 Sales Agreement, for aggregate net proceeds of $49.5 million after payment of cash commissions to the Sales Agent and legal, accounting and other fees in connection with the sales. During the three months ended June 30, 2021, we issued 641,709 shares of our common stock in a series of sales at an average price of $72.79 per share in accordance with the 2019 Sales Agreement, for aggregate net proceeds of $45.3 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. In June 2020, we issued 6,301,370 shares of our common stock, including the exercise in full by the underwriters of their option to purchase an additional 821,917 shares, at the public offering price of $18.25 per share pursuant to the 2019 Shelf for aggregate cash consideration of $107.7 million, after payment of commissions and fees and approximately $0.4 million related to legal, accounting and other fees in connection with the sales. In June 2020 we also issued 925,218 shares of our common stock to Regeneron in a private placement for an aggregate cash consideration of $30.0 million, or $32.42 per share, representing a 100% premium over the volume-weighted average trading price of the Company's common stock during the 30-day period prior to the closing. On November 30, 2020, we filed a Registration Statement on Form S-3ASR (the "Universal Shelf") with the SEC, which was automatically declared effective upon filing (File No. 333-251022) in relation to the registration of common stock, preferred stock, debt securities, warrants and units of any combination thereof. In December 2020, we issued 5,513,699 shares of our common stock, including the exercise in full by the underwriters of their option to purchase an additional 719,178 shares, at the public offering price of $36.50 per share pursuant to the Universal Shelf for aggregate cash consideration of $188.9 million, after deducting the underwriting discount, commissions and offering expenses. In July 2021, we issued 4,758,620 shares of our common stock, including the exercise in full by the underwriters of their option to purchase an additional 620,689 shares, at the public offering price of $145.00 per share pursuant to the Universal Shelf for aggregate cash consideration of approximately $648.3 million, after deducting the underwriting discount, commissions and estimated offering expenses. 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.

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. It cannot be predicted 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, 2020, we had federal and state NOLs of $372.5 million and $373.1 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, 2020, we had federal and state research and development and other credit carryforwards of approximately $15.0 million and $10.3 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. We may have experienced ownership changes in the past and may experience ownership changes in the future as a result of our initial public offering in May of 2016, follow-on offerings and/or subsequent shifts in our stock ownership (some of which shifts are outside our control). 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 6. Exhibits

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

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)

(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 4, 2021

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)

Exhibit 31.1

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

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

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

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

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

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

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

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

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

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

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

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

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

Date: November 4, 2021

/s/ John M. Leonard

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

Exhibit 31.2

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

I, 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 4, 2021

/s/ Glenn Goddard

Glenn Goddard
Executive Vice President, Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

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

In connection with this Quarterly Report on Form 10-Q of Intellia Therapeutics, Inc. (the "Company") for the period ended September 30, 2021, 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 4, 2021

/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)