

**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, 2020

OR

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

For the transition period from _____ to _____

Commission File Number: 001-37766

INTELLIA THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)

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

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

02139
(Zip Code)

857-285-6200

(Registrant's Telephone Number, Including Area Code)

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

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

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

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

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

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

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

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

The number of shares outstanding of the registrant's common stock as of October 30, 2020: 59,080,783 shares.

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PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

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

	September 30, 2020	December 31, 2019
ASSETS		
Current Assets:		
Cash and cash equivalents	\$ 179,746	\$ 57,226
Marketable securities	228,201	222,500
Accounts receivable	1,217	4,620
Prepaid expenses and other current assets	7,086	5,135
Total current assets	416,250	289,481
Marketable securities - noncurrent	-	4,746
Property and equipment, net	15,612	17,996
Operating lease right-of-use assets	22,210	19,137
Other assets	4,483	2,920
Total Assets	\$ 458,555	\$ 334,280
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	\$ 7,775	\$ 3,941
Accrued expenses	19,348	13,273
Current portion of operating lease liability	6,198	5,745
Current portion of deferred revenue	22,544	12,674
Total current liabilities	55,865	35,633
Deferred revenue, net of current portion	57,070	16,136
Long-term operating lease liability	16,000	12,630
Commitments and contingencies (Note 6)		
Stockholders' Equity:		
Common stock, \$0.0001 par value; 120,000,000 shares authorized; 58,792,212 and 50,198,044 shares issued and outstanding at September 30, 2020 and December 31, 2019, respectively	6	5
Additional paid-in capital	722,500	570,493
Accumulated other comprehensive income	31	261
Accumulated deficit	(392,917)	(300,878)
Total stockholders' equity	329,620	269,881
Total Liabilities and Stockholders' Equity	\$ 458,555	\$ 334,280

See notes to condensed consolidated financial statements.

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

	<u>Three Months Ended September 30,</u>		<u>Nine Months Ended September 30,</u>	
	<u>2020</u>	<u>2019</u>	<u>2020</u>	<u>2019</u>
Collaboration revenue	\$ 22,220	\$ 10,616	\$ 51,399	\$ 32,167
Operating expenses:				
Research and development	39,756	27,513	112,177	76,682
General and administrative	10,566	8,431	33,406	32,082
Total operating expenses	50,322	35,944	145,583	108,764
Operating loss	(28,102)	(25,328)	(94,184)	(76,597)
Interest income	262	1,694	2,145	5,340
Net loss	\$ (27,840)	\$ (23,634)	\$ (92,039)	\$ (71,257)
Net loss per share, basic and diluted	\$ (0.47)	\$ (0.49)	\$ (1.70)	\$ (1.53)
Weighted average shares outstanding, basic and diluted	58,754	48,554	54,218	46,547
Other comprehensive (loss) income:				
Unrealized (loss) gain on marketable securities	(124)	81	(230)	364
Comprehensive loss	\$ (27,964)	\$ (23,553)	\$ (92,269)	\$ (70,893)

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,	
	2020	2019
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	\$ (92,039)	\$ (71,257)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	4,709	4,021
Equity-based compensation	14,321	12,075
Accretion of investment discounts	(195)	(3,297)
Changes in operating assets and liabilities:		
Accounts receivable	3,403	3,948
Prepaid expenses and other current assets	(1,951)	(3,043)
Operating right-of-use assets	4,866	1,648
Other assets	348	110
Accounts payable	3,445	1,910
Accrued expenses	6,719	1,043
Deferred revenue	50,804	(20,788)
Operating lease liabilities	(4,116)	(948)
Net cash used in operating activities	(9,686)	(74,578)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	(2,579)	(4,222)
Purchases of marketable securities	(244,790)	(263,986)
Maturities of marketable securities	243,800	265,500
Net cash used in investing activities	(3,569)	(2,708)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of common stock through follow-on offering, net of issuance costs of \$0.4 million	107,732	-
Proceeds from issuance of common stock through at-the-market offerings, net of issuance costs of \$0.1 million and \$0.3 million, respectively	14,722	54,120
Proceeds from issuance of common stock to Regeneron	12,580	-
Proceeds from options exercised	1,967	2,216
Issuance of shares through employee stock purchase plan	685	534
Net cash provided by financing activities	137,686	56,870
Net increase (decrease) in cash and cash equivalents and restricted cash equivalents	124,431	(20,416)
Cash and cash equivalents and restricted cash equivalents, beginning of period	57,226	58,856
Cash and cash equivalents and restricted cash equivalents, end of period	<u>\$ 181,657</u>	<u>\$ 38,440</u>
Reconciliation of cash, cash equivalents and restricted cash equivalents to condensed consolidated balance sheet:		
Cash and cash equivalents	\$ 179,746	\$ 38,440
Restricted cash equivalents, included in other assets	1,911	-
Total cash, cash equivalents and restricted cash equivalents	<u>\$ 181,657</u>	<u>\$ 38,440</u>
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Purchases of property and equipment unpaid at period end	\$ 545	\$ 1,016
Right-of-use assets acquired under operating leases	7,939	2,554

See notes to condensed consolidated financial statements.

1. Overview and Basis of Presentation

Intellia Therapeutics, Inc. (“Intellia” or the “Company”) is a leading genome editing company, focused on the development of proprietary, potentially curative therapeutics using a biological tool known as CRISPR/Cas9, which stands for Clustered, Regularly Interspaced Short Palindromic Repeats (“CRISPR”)/CRISPR associated 9 (“Cas9”). This is a technology for genome editing, the process of altering selected sequences of genomic deoxyribonucleic acid (“DNA”). The Company believes the CRISPR/Cas9 technology has the potential to transform medicine by both producing therapeutics that permanently edit and/or correct disease-associated genes in the human body with a single treatment course, and creating enhanced engineered cells that can treat oncological and immunological diseases. The Company’s combination of deep scientific, technical and clinical development experience, along with its intellectual property (“IP”) portfolio, puts it in a position to unlock broad therapeutic applications of the CRISPR/Cas9 technology and create new classes of therapeutic products.

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 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, 2019.

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 gain/loss on marketable securities.

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 and equity-based compensation expense. The Company bases its estimates on historical experience and various other assumptions that management believes to be reasonable under the circumstances at the time such estimates are made. Actual results could differ from those estimates. The Company periodically reviews its estimates in light of changes in circumstances, facts and experience. The 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 our 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. Certain prior year amounts have been reclassified in order to conform to the current year presentation.

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, 2020, the Company has raised an aggregate of \$893.6 million to fund its operations, of which \$272.6 million was through its collaboration agreements, \$170.5 million was from its initial public offering (“IPO”) and concurrent private placements, \$249.1 million was from follow-on public offerings, \$116.4 million was from at-the-market offerings and \$85.0 million was from the sale of convertible preferred stock. The Company expects that its cash, cash equivalents and marketable securities as of September 30, 2020, as well as research and cost reimbursement funding from its collaboration agreement with Regeneron (see Note 7), 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, 2019. There have been no material changes during the nine months ended September 30, 2020, other than as noted below.

Restricted Cash Equivalents

Restricted cash equivalents are money market funds held in collateral accounts that are restricted to secure a letter of credit in accordance with the lease for 281 Albany Street that the Company entered into in March of 2020 (see Note 8). The letter of credit is required to be maintained throughout the term of the lease, which is ten years. These restricted cash equivalents amount to \$1.9 million and are included in “Other Assets” in the Company’s condensed consolidated balance sheet.

Recent Accounting Pronouncements – Adopted

In August 2018, the Financial Accounting Standards Board (“FASB”) issued Accounting Standards Update (“ASU”) 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement* (“ASU 2018-13”). The new standard modifies disclosure requirements related to fair value measurement. The Company adopted ASU 2018-13 on January 1, 2020. The adoption did not have a material impact on the Company’s condensed consolidated financial statements as of and for the three or nine months ended September 30, 2020.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* (“ASU 2016-13”). The standard changes how credit losses are measured for most financial assets and certain other instruments. For trade and other receivables, the standard requires the use of a new forward-looking “expected credit loss” model that generally will result in the earlier recognition of allowances for losses. For available-for-sale debt securities with unrealized losses, the standard now requires allowances to be recorded instead of reducing the amortized cost of the investment. With certain exceptions, the guidance is applied using a modified retrospective approach by reflecting adjustments through a cumulative-effect impact to retained earnings as of the beginning of the fiscal year of adoption. The Company adopted ASU 2016-13 on January 1, 2020. The adoption did not have a material effect on the Company’s condensed consolidated financial statements as of and for the three or nine months ended September 30, 2020.

Recent Accounting Pronouncements – Issued but not yet adopted

In December 2019, the FASB issued 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 amendments in ASU 2019-12 are effective for fiscal years beginning after December 15, 2020, including interim periods therein. Early adoption of the standard is permitted. The Company does not anticipate that the adoption of ASU 2019-12 will 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, 2020 and December 31, 2019 at net book value:

	September 30, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
(In thousands)				
Marketable securities:				
U.S. Treasury securities	\$ 79,962	\$ 5	\$ -	\$ 79,967
Financial institution debt securities	111,265	35	(5)	111,295
Corporate debt securities	31,832	-	(6)	31,826
Other asset-backed securities	5,111	2	-	5,113
Total	<u>\$ 228,170</u>	<u>\$ 42</u>	<u>\$ (11)</u>	<u>\$ 228,201</u>

	December 31, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
(In thousands)				
Marketable securities:				
U.S. Treasury securities	\$ 159,361	\$ 142	\$ (1)	\$ 159,502
Financial institution debt securities	40,173	105	-	40,278
Corporate debt securities	18,966	1	-	18,967
Other asset-backed securities	8,485	14	-	8,499
Total	<u>\$ 226,985</u>	<u>\$ 262</u>	<u>\$ (1)</u>	<u>\$ 227,246</u>

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At September 30, 2020 and December 31, 2019, the balance in the Company's accumulated other comprehensive income was composed of activity related to the Company's available-for-sale marketable securities. There were no material realized gains or losses in the nine months ended September 30, 2020 or for the year ended December 31, 2019. The Company did not reclassify any amounts out of accumulated other comprehensive income during this period. The Company did not have any securities in a material unrealized loss position at September 30, 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, 2020 and December 31, 2019, 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 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, 2020 and December 31, 2019, the Company's financial assets recognized at fair value on a recurring basis consisted of the following:

	Fair Value as of September 30, 2020			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	\$ 172,407	\$ 172,407	\$ -	\$ -
Marketable securities:				
U.S. Treasury securities	79,967	79,967	-	-
Financial institution debt securities	111,295	-	111,295	-
Corporate debt securities	31,826	-	31,826	-
Other asset-backed securities	5,113	-	5,113	-
Total marketable securities	228,201	79,967	148,234	-
Total	\$ 400,608	\$ 252,374	\$ 148,234	\$ -

	Fair Value as of December 31, 2019			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	\$ 46,917	\$ 46,917	\$ -	\$ -
Marketable securities:				
U.S. Treasury securities	159,502	159,502	-	-
Financial institution debt securities	40,278	-	40,278	-
Corporate debt securities	18,967	-	18,967	-
Other asset-backed securities	8,499	-	8,499	-
Total marketable securities	227,246	159,502	67,744	-
Total	\$ 274,163	\$ 206,419	\$ 67,744	\$ -

The Company's financial assets, which include 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 our validation procedures, the Company did not adjust or override any fair value measurements provided by the pricing services as of September 30, 2020 or December 31, 2019.

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

5. Accrued Expenses

Accrued expenses consisted of the following:

	September 30, 2020	December 31, 2019
(In thousands)		
Employee compensation and benefits	\$ 8,642	\$ 6,311
Accrued research and development	6,396	4,208
Accrued legal and professional expenses	2,024	1,563
Accrued other	2,286	1,191
Total accrued expenses	\$ 19,348	\$ 13,273

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, 2019. 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, 2019.

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, 2020, 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, 2020, the Company's accounts receivable and contract liabilities were related to the Company's collaboration with Regeneron Pharmaceuticals, Inc. ("Regeneron"). As of September 30, 2019, the Company's accounts receivable and contract liabilities were related to the Company's collaborations with Regeneron and Novartis Institutes for BioMedical Research ("Novartis").

The following table presents changes in the Company's accounts receivable and contract liabilities during the nine months ended September 30, 2020 and 2019 (in thousands):

	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
	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Nine Months Ended September 30, 2019				
Accounts receivable	\$ 7,547	\$ 11,379	\$ (15,327)	\$ 3,599
Contract liabilities:				
Deferred revenue	\$ 55,932	\$ 3,000	\$ (23,788)	\$ 35,144

During the nine months ended September 30, 2020 and 2019, the Company recognized the following revenues as a result of changes in the contract liability balance (in thousands):

Revenue recognized in the period from:	Nine Months Ended September 30,	
	2020	2019
Amounts included in the contract liability at the beginning of the period	\$ 10,249	\$ 23,788

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.

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.

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 “2020 Stock Purchase Agreement”).

2016 Regeneron Agreement: Scope. Under the initial six-year term of the 2016 Regeneron Agreement, Regeneron obtained exclusive rights for up to ten targets (the “Regeneron Target Cap”) to be chosen by Regeneron during the Technology Collaboration Term, as defined in the 2016 Regeneron Agreement, subject to a target selection process and various adjustments and limitations set forth in the 2016 Regeneron Agreement. Of these ten total targets, Regeneron may select up to five non-liver targets, while the remaining targets must be focused in the liver. The Company retains the exclusive right to solely develop certain *in vivo* products directed against specified genetic targets as well as certain non-liver targets from the Company’s ongoing and planned research activities. During the collaboration term, and subject to a target selection process, the Company has the right to choose additional liver targets for its own development using commercially reasonable efforts. Certain targets that either the Company or Regeneron select during the collaboration term may be subject to co-development and co-promotion (“Co/Co”) agreements at the Company or Regeneron’s option. Regeneron has the option to enter into Co/Co agreements for up to five liver targets (other than the Company’s reserved liver targets) and the Company has the option to enter into one Intellia Independent Co/Co Option (as defined in the 2016 Regeneron Agreement). At the inception of the 2016 Regeneron Agreement, Regeneron selected the first of its ten targets, transthyretin amyloidosis (“ATTR”), which is subject to a Co/Co agreement between the Company and Regeneron (the “ATTR Co/Co”). The general terms and conditions for the ATTR Co/Co were outlined within the 2016 Regeneron Agreement.

In addition, the Company granted Regeneron a non-exclusive, worldwide license, 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.

2016 Regeneron Agreement: Financial Terms. In connection with the 2016 Regeneron Agreement, the Company received a nonrefundable upfront payment of \$75.0 million. In addition, on Regeneron programs that are not subject to Co/Co agreements, the Company may be eligible to earn, on a per-licensed target basis, (i) up to \$25.0 million in development milestones, including for the dosing of the first patient in each of Phase I, Phase II and Phase III clinical trials, (ii) up to \$110.0 million in regulatory milestones, including for the acceptance of a regulatory filing in the U.S., and for obtaining regulatory approval in the U.S. and in certain other identified countries and (iii) up to \$185.0 million in sales-based milestone payments. The Company is also eligible to earn royalties ranging from the high-single digits to low teens, in each case, on a per-product basis, which royalties are potentially subject to various reductions and offsets and incorporate the Company’s existing low- to mid-single-digit royalty obligations under a license agreement with Caribou Biosciences, Inc. (“Caribou”). In connection with the 2016 Regeneron Agreement, Regeneron purchased \$50.0 million of the Company’s common stock in a private placement under a stock purchase agreement concurrent with the Company’s IPO.

2020 Regeneron Amendment: Scope. The 2020 Regeneron Amendment, among other things, (i) extends the Technology Collaboration Term until April 11, 2024, with a further option to extend an additional twenty-four months upon notice and a \$30.0 million nonrefundable payment to the Company, (ii) increases the Regeneron Target Cap from ten to fifteen (with the additional five targets focused only in the liver) and (iii) allows for a second Intellia Independent Co/Co Option. The Company also granted a non-exclusive license to Regeneron under certain CRISPR/Cas platform IP for the commercialization of up to ten *ex vivo* edited CRISPR Products (as defined in the 2020 Regeneron Amendment) made using certain cell types, subject to certain limitations on Regeneron’s activities in T cells. The *ex vivo* license does not include access to the Company’s IP directed to its *ex vivo* targets, programs, or cell engineering processes. This non-exclusive license is subject to royalty obligations such that the Company is eligible to earn royalties on *ex vivo* edited CRISPR Products ranging from the high-single

digits to low teens, in each case, on a per-product basis, subject to various reductions and offsets and the Company's existing royalty obligations to Caribou. The Company transferred the license to develop the Factor VIII target for the treatment of hemophilia A to Regeneron. In addition, a target that was previously a Regeneron evaluation target was transferred back to the Company as an Intellia reserved liver target with certain reserved rights for Regeneron.

In connection with the 2020 Regeneron Amendment, the Company and Regeneron also entered into the Hemophilia Co/Co agreements, which are directed to Factor VIII and Factor IX for the treatment of hemophilia A and hemophilia B. Factor VIII and Factor IX do not count toward the Regeneron Target Cap. Under the Hemophilia Co/Co agreements, which are substantially based upon the terms and conditions as outlined under the 2016 Regeneron Agreement, the Company and Regeneron will collaborate to research, develop, manufacture, and commercialize CRISPR Products for the treatment of hemophilia A and hemophilia B, for which Regeneron will be the Lead Party (as discussed below). Further, worldwide development costs and profits of any future products will be split between the Company and Regeneron, 35% and 65%, respectively, subject to certain deductions.

2020 Regeneron Amendment: Financial Terms. As part of the consideration for the 2020 Regeneron Amendment, Regeneron paid the Company an upfront payment of \$70.0 million, which included the \$25.0 million fee to extend the Technology Collaboration Term to April 2024. The potential future milestones and royalties remain unchanged from the 2016 Regeneron Agreement. In addition, on May 30, 2020, the Company and Regeneron entered into the 2020 Stock Purchase Agreement. Under the 2020 Stock Purchase Agreement, the Company sold to Regeneron 925,218 shares of its common stock, par value \$0.0001 per share, for aggregate cash consideration of \$30.0 million, or \$32.42 per share (the "Equity Transaction"), 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 of the Equity Transaction. Under the 2020 Stock Purchase Agreement, Regeneron will not dispose of any shares of common stock it beneficially owns in the Company until the termination of the Technology Collaboration Term.

Research Collaboration. Research activities under the 2016 Regeneron Agreement and the 2020 Regeneron Amendment (collectively the "Amended Agreements") will be governed by evaluation and research and development plans that will outline the parties' responsibilities under, anticipated timelines of and budgets for, the various programs. The Company will assist Regeneron with the preliminary evaluation of its selected *in vivo* targets, and Regeneron will be responsible for preclinical research, conducting clinical development and manufacturing and commercialization of CRISPR Products directed to each of its exclusive selected targets. The Company may assist, as requested by Regeneron, with the later discovery and research of product candidates directed to any selected target. For each selected target, Regeneron is required to use commercially reasonable efforts to submit regulatory filings necessary to achieve investigational new drug ("IND"), or other regulatory acceptance for at least one product directed to each applicable target and, following IND or other regulatory acceptance, to develop and commercialize at least one such product.

Governance. Pursuant to the 2016 Regeneron Agreement, the parties formed a joint steering committee, which is responsible for setting research objectives and overseeing the general strategies and research and development activities undertaken by the parties.

Term and Termination. Under the Amended Agreements, the Technology Collaboration Term ends in April 2024, except that Regeneron may make a one-time payment of \$30.0 million to extend the Technology Collaboration Term for an additional two-year period. The Amended Agreements will continue until the date when no royalty or other payment obligations are due, unless earlier terminated in accordance with the terms of the Amended Agreements. Regeneron's royalty payment obligations expire on a country-by-country and product-by-product basis upon the later of (i) the expiration of the last valid claim of the royalty-bearing patents covering such product in such country, (ii) twelve years from the first commercial sale of such product in such country, or (iii) the expiration of regulatory exclusivity for such product. The Company may terminate the Amended Agreements on a target-by-target basis if Regeneron or any of its affiliates institutes a patent challenge against the Company's CRISPR/Cas or certain other background patent rights or does not proceed with the development of a product directed to a selected target within specified periods of time. Regeneron may terminate the Amended Agreements, without cause, upon 180 days written notice to the Company, either in its entirety or on a target-by-target basis, in which event, certain rights in the terminated targets and associated IP revert to the Company, as described in the Amended Agreements. Following such termination, the Company may owe Regeneron royalties, in certain circumstances, up to mid-single digits on any terminated targets that the Company subsequently commercializes on a product-by-product basis for a period of twelve years after the first commercial sale of any such products. Either party may terminate the Amended Agreements, either in their entirety or with

respect to the research collaboration or one or more of the targets selected by Regeneron, in the event of the other party's uncured material breach.

Co-Development and Co-Promotion Agreements. In July 2018, the Company and Regeneron finalized the form of the Co/Co agreement that will be used as the basis for each Co/Co agreement directed to a target. Simultaneously, the Company and Regeneron executed the ATTR Co/Co agreement, for which the Company is the clinical and commercial Lead Party and Regeneron is the Participating Party (each, as defined in the Co/Co agreements, as applicable, and described below). In May 2020, the Company and Regeneron executed the Hemophilia Co/Co agreements, for which Regeneron is the clinical and commercial Lead Party and the Company is the Participating Party.

Co-Development and Co-Promotion: Agreement Structure. Under the 2016 Regeneron Agreement, Regeneron had the right to exercise at least four options, after ATTR, to enter into a Co/Co agreement for the Company's liver targets (other than the Company's reserved liver targets), while the Company had the opportunity to exercise at least one option to enter into a Co/Co agreement for Regeneron's liver targets, the exact number of options being subject to certain conditions of the target selection process. In connection with the 2020 Regeneron Amendment, the Company received one additional option to enter into a Co/Co agreement, while Regeneron's number of Co/Co options remained the same. Each option to enter into a Co/Co agreement must be exercised (or forfeited) once a target reaches a defined preclinical stage. One party will be the "Lead Party" and the other party the "Participating Party." The Lead Party will have control and primary responsibility for the development, manufacturing, regulatory, and commercial activities. The Participating Party will have the right to consult on these activities through its participation on the joint development and commercialization committees and will have the right to co-fund development and commercialization activities in exchange for a share of profits. In general, under each Co/Co agreement, the parties will share equally in worldwide development costs and profits of any future products. Prior to reaching a specific development milestone, the Participating Party may elect to reduce its share of worldwide development costs and profits by 50%. Pursuant to the ATTR Co/Co, on December 13, 2019, Regeneron informed the Company that it would exercise its rights under the ATTR Co/Co agreement to modify its share of worldwide development costs and profits from 50% to 25%, effective in mid-June 2020.

As noted above, in connection with the 2020 Regeneron Amendment, the Company and Regeneron entered into two Hemophilia Co/Co agreements. Under the Hemophilia Co/Co agreements, which are substantially based upon the Company and Regeneron's previously agreed-upon form of Co/Co agreement, but do not count toward Regeneron's total number of Co/Co options, the Company and Regeneron will collaborate to research, develop, manufacture, and commercialize CRISPR Products for the treatment of hemophilia A and hemophilia B. Regeneron will be the clinical and commercial lead for such activities.

Co-Development and Co-Promotion: Governance. The parties formed joint development and commercialization committees to oversee all profit share products under the Co/Co agreements as discussed below. The committees are responsible for overseeing the development, manufacture, regulatory matters, and commercialization (including pricing and reimbursement) efforts under the ATTR Co/Co and the Hemophilia Co/Co agreements.

Co-Development and Co-Promotion: Termination. Either party may terminate a particular Co/Co agreement by providing 180 days written notice. If the Company terminates, the product subject to the Co/Co agreement becomes a Regeneron product, and is subject to all future milestone and royalty payment obligations under the 2016 Regeneron Agreement. If Regeneron terminates and has contributed at least \$5.0 million in development costs under the particular Co/Co agreement, the Company will pay low- to mid-single-digit royalties on the net sales of the product, depending on co-funding percentage, stage at termination and, if any, Regeneron IP incorporated into the relevant product.

2016 Regeneron Agreement: Accounting Analysis. The Company determined that the 2016 Regeneron Agreement 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 2016 Regeneron Agreement and determined that it included three performance obligations: (i) a combined performance obligation including the licenses to targets and the associated research activities and evaluation plans; (ii) a combined performance obligation including the technology collaboration and associated research activities; and (iii) the common stock.

Under the 2016 Regeneron Agreement, the Company determined that the transaction price was \$125.0 million, consisting of the following consideration: (i) the nonrefundable upfront payment of \$75.0 million; and (ii) the payment of the common stock of \$50.0 million. None of the clinical or regulatory milestones were included in the transaction price, as all milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future regulatory progress and the licensee's efforts. Any consideration related to sales-based milestones and royalties will be recognized when the related sales occur as they were determined to relate predominantly to the licenses granted to Regeneron and therefore have also been excluded from the transaction price.

The Company first allocated \$50.0 million of the transaction price to the common stock. The common stock was sold at its standalone selling price and the Company concluded that the total discount inherent in the arrangement is entirely attributable to the combined performance obligation including the licenses to targets and associated research activities and evaluation plans and the combined performance obligation including the technology collaboration and associated research activities. As such, the remaining \$75.0 million of the transaction price was allocated to the combined performance obligation including the licenses to targets and associated research activities and evaluation plans and the combined performance obligation including the technology collaboration and associated research activities on a relative standalone selling price basis. The Company estimated the standalone selling price of each combined performance obligation by taking into consideration internal estimates of research and development personnel needed to perform the research and development services, estimates of expected cash outflows to third parties for services and supplies, selling prices of comparable transactions and typical gross profit margins. As a result of this evaluation, the Company allocated \$63.8 million to the combined performance obligation including the licenses to targets and associated research activities and evaluation plans and \$11.2 million to the combined performance obligation including the technology collaboration and associated research activities. The \$63.8 million allocated to the combined performance obligation including the licenses to targets and associated research activities and evaluation plans is being recognized using a time elapsed inputs method over a period of six years, which, in management's judgment, 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 Regeneron and represents the Company's best estimate of the period of the obligation. The \$11.2 million allocated to the combined performance obligation including the technology collaboration and associated research activities is being recognized using a time elapsed inputs method over a period beginning with the inception of the technology collaboration in September 2016 through the end of the arrangement, which, in management's judgment, 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 Regeneron and represents the Company's best estimate of the period of the obligation.

2020 Regeneron Amendment: Accounting Analysis. The Company concluded that the accounting for the 2020 Regeneron Amendment is within the scope of ASC 606. The Company evaluated the promised goods and services under the 2020 Regeneron Amendment and determined that it included three performance obligations: (i) a combined performance obligation including the licenses to targets and the associated research activities and evaluation plans; (ii) a combined performance obligation including the technology collaboration and associated research activities; and (iii) the transfer of the license to develop the Factor VIII target for hemophilia A. The 2020 Regeneron Amendment represents a contract modification. The modification of the license to targets and the associated research activities and evaluation plans and the license to the technology collaboration and associated research activities are accounted for as if they were part of the original agreement and therefore form part of a performance obligation that was partially satisfied at the date of modification. The Company therefore recorded a cumulative catch-up adjustment of \$8.4 million on the modification date. The Company accounted for the distinct performance obligation – specifically the obligation to transfer the license to develop the Factor VIII target for hemophilia A - as if it were a separate component of the modified contract.

The transaction price of the 2020 Regeneron Amendment was determined to be \$110.9 million, which is comprised of the \$23.5 million remaining consideration from the 2016 Regeneron Agreement transferred at the inception of the arrangement, the \$70.0 million upfront payment received upon the execution of the 2020 Regeneron Amendment and \$17.4 million on the sale of shares under the 2020 Stock Purchase Agreement. The Company applied equity accounting guidance to measure the \$12.6 million fair value recorded in the condensed consolidated statement of stockholders' equity upon issuance of the shares. All variable consideration will be fully constrained, until such point where the constraints can be lifted, at which point the Company will allocate the consideration to the performance obligations in the arrangement accordingly.

The \$110.9 million transaction price was allocated to the performance obligations including the licenses to targets and associated research activities and evaluation plans, the combined performance obligation including the technology collaboration and associated research activities and the transfer of the license to develop the Factor VIII target for hemophilia A, on a relative standalone selling price basis. The Company estimated the standalone selling price of the transfer of the license to develop the Factor VIII target for hemophilia A using the adjusted market assessment approach, whereby the Company estimated the market in which it sells goods or services and estimated the price that a customer in that market would be willing to pay for those goods or services. The Company estimated the standalone selling price of the combined performance obligation of the technology collaboration and associated research activities by taking into consideration internal estimates of research and development personnel needed to perform the research and development services. The estimated standalone selling price of the combined performance obligation, including the licenses to targets and the associated research activities and evaluation plans, was determined using selling prices of comparable transactions.

As a result of this evaluation, the Company allocated \$91.9 million to the combined performance obligation including the licenses to targets and associated research activities and evaluation plans, \$3.7 million to the combined performance obligation including the technology collaboration and associated research activities, and \$15.3 million to the transfer of the license to develop the Factor VIII target for hemophilia A.

The \$91.9 million allocated to the combined performance obligation, including the licenses to targets and associated research activities and evaluation plans, as well as the \$3.7 million allocated to the combined performance obligation, including the technology collaboration and associated research activities, are being recognized using a time elapsed inputs method over the remaining period of the collaboration which, in management's judgment, 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 Regeneron and represents the Company's best estimate of the period of the obligation. The Company will re-evaluate the measure of progress in each reporting period and when events whose outcome are resolved or other changes in circumstances occur. The \$15.3 million allocated to the transfer of the license to develop the Factor VIII target for hemophilia A was recognized when the Company transferred control of the hemophilia A target during the quarter ended September 30, 2020.

Co/Co Agreements: Accounting Analysis. The Company concluded that the ATTR Co/Co and Hemophilia Co/Co agreements meet the definition of a collaborative arrangement per Accounting Standards Codification 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 ATTR Co/Co and the Hemophilia Co/Co agreements 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.

Revenue Recognition – Collaboration Revenue. Through September 30, 2020, 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 \$33.8 million primarily for research and development services under the ATTR Co/Co agreement. Through September 30, 2020, the Company has recognized \$116.7 million of collaboration revenue under all arrangements, including \$22.2 million and \$46.4 million during the three and nine months ended September 30, 2020, respectively, and \$5.8 million and \$17.8 million during the three and nine months ended September 30, 2019, respectively, in the condensed consolidated statements of operations and comprehensive loss. This includes \$1.2 million and \$9.8 million during the three and nine months ended September 30, 2020, respectively, and \$2.6 million and \$8.4 million during the three and nine months ended September 30, 2019, respectively, primarily representing payments due from Regeneron pursuant to the ATTR Co/Co agreement.

As of September 30, 2020, there was approximately \$79.6 million of the aggregate transaction price of the Amended Agreements remaining to be recognized, which the Company expects to be recognized ratably through April 2024.

As of September 30, 2020 and December 31, 2019, the Company had accounts receivable of \$1.2 million and \$3.6 million, respectively, and deferred revenue of \$79.6 million and \$28.8 million, respectively, related to the Amended Agreements.

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 chimeric antigen receptor T (“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. Since December 31, 2019, there have been no 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, 2019.

Revenue Recognition – Collaboration Revenue. Through September 30, 2020, excluding amounts allocated to Novartis’ purchase of the Company’s Class A-1 and Class A-2 Preferred Units, the Company had recorded a total of \$62.4 million in cash under the 2014 Novartis Agreement and the Novartis Amendment. Through September 30, 2020, the Company recognized \$62.4 million of collaboration revenue. No revenue was recognized during the three or nine months ended September 30, 2020 related to the 2014 Novartis Agreement and the Novartis Amendment. The Company recognized \$4.8 million and \$14.3 million during the three and nine months ended September 30, 2019, in the condensed consolidated statements of operations and comprehensive loss related to the 2014 Novartis Agreement and the Novartis Amendment. As of December 31, 2019, the aggregate transaction price had been recognized in full.

Revenue Recognition – Milestone. During the nine months ended September 30, 2020, the U.S. Food and Drug Administration (“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, the Company recognized \$5.0 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, 2020 or 2019. The Company is eligible to receive additional downstream success-based milestones and royalties.

As of September 30, 2020, the Company had no accounts receivable related to the 2014 Novartis Agreement and the Novartis Amendment. As of December 31, 2019, the Company had accounts receivable of \$1.0 million related to the 2014 Novartis Agreement and the Novartis Amendment. As of September 30, 2020 and December 31, 2019, the Company had no deferred revenue related to the 2014 Novartis Agreement and the Novartis Amendment.

8. Leases

In October 2014, the Company entered into an agreement to lease office and laboratory space at 130 Brookline Street (the “130 Brookline Lease”) in Cambridge, Massachusetts under an operating lease agreement with a term through January 2020, with an option to extend the term of the lease for an additional five-year period. In April 2019, the Company executed an amendment to the lease to extend the term of the lease for the additional five-year period, through January 2025. Upon the execution of the original lease, the Company provided a \$0.3 million security deposit. The Company has recorded this security deposit in other assets on the condensed consolidated balance sheets. In March 2020, the Company entered into a second amendment to the 130 Brookline Lease (the “Second Amendment”). The Second Amendment amends certain terms of the Company’s existing lease, dated October 21, 2014, as amended on April 5, 2019. The Second Amendment extends the term of the 130 Brookline Lease by approximately six years through January 31, 2031. This extended term is included as part of the lease liability and right-of-use asset at September 30, 2020. The Second Amendment also provides an option to extend the lease for two consecutive five-year terms. In the first quarter of 2020, the Company recognized a right-of-use asset and lease liability of approximately \$7.3 million related to the Second Amendment.

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. As of September 30, 2020 the Company determined, in accordance with Accounting Standards Codification 842, “Leases (Topic 842)”, that the lease commencement date has not been met as the Company does not control the underlying asset. 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 will 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 sheet. The Company has the option to extend the 281 Albany Lease for two successive five-year terms.

9. 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, 2020, there were 2,144,877 shares available for future issuance. The number of shares reserved for issuance under the 2015 Plan shall be cumulatively increased by four percent of the number of shares of stock issued and outstanding on the immediately preceding December 31 or such lesser number of shares of 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,	
	2020	2019	2020	2019
	(In thousands)			
Research and development	\$ 2,775	\$ 1,513	\$ 7,325	\$ 5,392
General and administrative	2,625	1,566	6,996	6,683
Total	<u>\$ 5,400</u>	<u>\$ 3,079</u>	<u>\$ 14,321</u>	<u>\$ 12,075</u>

Restricted Stock

Restricted stock is 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, 2020:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Unvested restricted stock as of December 31, 2019	71,875	\$ 22.88
Granted	181,020	15.05
Vested	-	-
Cancelled	(28,369)	21.66
Unvested restricted stock as of September 30, 2020	<u>224,526</u>	<u>\$ 16.72</u>

As of September 30, 2020, there was \$1.7 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 1.5 years. As of September 30, 2020, 47,916 of the unvested restricted stock outstanding are performance-based RSUs that vest upon obtaining certain scientific and regulatory milestones through 2020. During the three months ended September 30, 2020, 23,959 performance-based RSUs were cancelled as the performance criteria had not been met as of the milestone measurement date. The outstanding performance-based RSUs are not included in computing the diluted loss per share because the performance criteria had not been met as of the end of the reporting period.

In January 2020, the Company granted 181,020 RSUs to certain non-executive employees that include a performance condition in addition to a service condition. The RSUs vest over a period of three years and are subject to accelerated vesting based on the Company's programs achieving certain development milestones before December 1, 2022. The fair value of the RSUs at date of grant was \$15.05. As of September 30, 2020, the Company had not accelerated the vesting of the RSUs.

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 \$13.38 and \$8.55 per option for those options granted during the three and nine months ended September 30, 2020 and \$9.66 and \$9.21 per option for those options granted during the three and nine months ended September 30, 2019, 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, 2020 was \$0.9 million and \$1.7 million, respectively, and during the three and nine months ended September 30, 2019 was \$0.2 million and \$1.6 million, respectively. Key assumptions used to apply this pricing model were as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Risk-free interest rate	0.4%	1.6%	0.9%	2.2%
Expected life of options	6.0 years	6.0 years	5.5-6.0 years	5.5-6.0 years
Expected volatility of underlying stock	70.8%	67.5%	67.6%	68.3%
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 average historical stock volatilities of several peer companies within the Company's industry and the Company's historical volatility, 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, 2020:

	Number of Options	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Outstanding at December 31, 2019	5,365,971	\$ 15.67		
Granted	2,797,065	14.20		
Exercised	(205,184)	9.64		
Forfeited	(430,998)	18.21		
Outstanding at September 30, 2020	<u>7,526,854</u>	\$ 15.14	7.93	\$ 40,456
Exercisable at September 30, 2020	<u>3,296,341</u>	\$ 14.95	6.63	\$ 19,191

As of September 30, 2020, there was \$35.5 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 2.6 years.

Of the unvested stock options outstanding as of September 30, 2020, 135,832 are performance-based stock options that vest upon obtaining certain scientific and regulatory milestones through 2020. During the nine months ended September 30, 2020, 77,918 performance-based options were cancelled as the performance criteria had not been met as of the milestone measurement date. At September 30, 2020, 95,832 performance-based options are not included in computing the diluted loss per share because the performance criteria had not been met as of the end of the reporting period.

10. 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,	
	2020	2019	2020	2019
	(In thousands)			
Net loss	\$ (27,840)	\$ (23,634)	\$ (92,039)	\$ (71,257)
Weighted average shares outstanding, basic and diluted	58,754	48,554	54,218	46,547
Net loss per share, basic and diluted	<u>\$ (0.47)</u>	<u>\$ (0.49)</u>	<u>\$ (1.70)</u>	<u>\$ (1.53)</u>

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

	Three and Nine Months Ended September 30,	
	2020	2019
	(In thousands)	
Unvested restricted stock	225	72
Stock options	<u>7,527</u>	<u>5,408</u>
	<u>7,752</u>	<u>5,480</u>

11. Stockholders' Equity

The following tables present changes in stockholders' equity for the nine-month periods ended September 30, 2020 and 2019 (in thousands, except share data):

	Common		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2019	50,198,044	\$ -	\$ 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

	Common		Additional Paid-In Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2018	45,224,480	\$ 5	\$ 478,968	\$ (28)	\$ (201,025)	\$ 277,920
Retroactive adjustment to beginning accumulated deficit for adoption of ASC 842	-	-	-	-	(320)	(320)
Issuance of common stock through at-the-market offerings, net of issuance costs of \$120	223,818	-	3,639	-	-	3,639
Exercise of stock options	30,800	-	360	-	-	360
Equity-based compensation	-	-	4,592	-	-	4,592
Other comprehensive income	-	-	-	87	-	87
Net loss	-	-	-	-	(21,940)	(21,940)
Balance at March 31, 2019	45,479,098	\$ 5	\$ 487,559	\$ 59	\$ (223,285)	\$ 264,338
Issuance of common stock through at-the-market offerings, net of issuance costs of \$3	1,986,579	-	31,413	-	-	31,413
Exercise of stock options	203,072	-	1,664	-	-	1,664
Issuance of shares under employee stock purchase plan	45,826	-	534	-	-	534
Equity-based compensation	-	-	4,404	-	-	4,404
Other comprehensive income	-	-	-	196	-	196
Net loss	-	-	-	-	(25,683)	(25,683)
Balance at June 30, 2019	47,714,575	\$ 5	\$ 525,574	\$ 255	\$ (248,968)	\$ 276,866
Issuance of common stock through at-the-market offerings, net of issuance costs of \$199	1,141,411	-	19,068	-	-	19,068
Exercise of stock options	21,311	-	192	-	-	192
Equity-based compensation	-	-	3,079	-	-	3,079
Other comprehensive gain	-	-	-	81	-	81
Net loss	-	-	-	-	(23,634)	(23,634)
Balance at September 30, 2019	48,877,297	\$ 5	\$ 547,913	\$ 336	\$ (272,602)	\$ 275,652

Follow-on Offering

On June 1, 2020, the Company entered into an underwriting agreement related to a public offering of 6,301,370 shares of its common stock, par value \$0.0001 per share, 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. The offering closed on June 5, 2020 and the Company received net proceeds of \$107.7 million, after deducting the underwriting discount, commissions and approximately \$0.4 million in offering expenses.

Shares Issued in Private Placement to Regeneron

As described in Note 7 above, in May 2020 the Company entered into an amendment to its collaboration agreement with Regeneron that was entered into in April 2016. Simultaneously, the Company and Regeneron entered into the 2020 Stock Purchase Agreement, under which the Company sold to Regeneron 925,218 shares of its common stock, par value \$0.0001 per share, for 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. Under the 2020 Stock Purchase Agreement, Regeneron will not dispose of any shares of common stock it beneficially owns in the Company until the termination of the Technology Collaboration Term (see Note 7). After applying equity accounting guidance to measure the issuance of the shares, \$12.6 million was recorded as fair value in the condensed consolidated statement of stockholders' equity for the shares.

At-the-Market Offering Programs

In October 2018, the Company entered into an Open Market Sale Agreement (the "2018 Sales Agreement") with Jefferies LLC ("Jefferies"), under which Jefferies was able to offer and sell, from time to time in "at-the-market" offerings, shares of its common stock having aggregate gross proceeds of up to \$100.0 million. The Company paid to Jefferies cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2018 Sales Agreement. The Company issued 5,890,648 shares of its common stock at an average price of \$16.98 per share in accordance with the 2018 Sales Agreement for aggregate net proceeds of \$96.4 million, after payment of cash commissions to Jefferies and approximately \$0.6 million related to legal, accounting and other fees in connection with the sales. All shares related to the 2018 Sales Agreement had been sold as of December 31, 2019.

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. During the year ended December 31, 2019, the Company issued 287,231 shares of its common stock, in a series of sales, 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 Jefferies and approximately \$0.2 million related to legal, accounting and other fees in connection with the sales. 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, 2020, \$130.0 million in shares of common stock remain eligible for sale under the 2019 Sales Agreement.

12. 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.

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;
- the anticipated timing of preclinical studies, manufacturing activities and our investigational new drug application ("IND") or equivalent regulatory filing for NTLA-5001, our program for the treatment of acute myeloid leukemia;
- the anticipated timing of preclinical studies, manufacturing activities and our IND application or equivalent regulatory filing for NTLA-2002, our program for the treatment of hereditary angioedema;
- our ability to use a modular platform capability or other strategy 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;
- our ability to manufacture or obtain material 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 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 collaboration agreements and our ability to enter into strategic arrangements;
- our ability to maintain and establish collaborations with third parties 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 from which we derive rights, collaborators, competitors and our industry;*
- *the effect of the coronavirus disease 2019 (“COVID-19”) pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations;*
- *our ability to agree to terms with Caribou Biosciences, Inc. (“Caribou”) in accordance with the September 2019 interim award issued by the arbitration panel in our arbitration against Caribou (the “Caribou Arbitration”), including the scope and potential payments of such arrangement; 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 genome editing company, focused on the development of proprietary, potentially curative therapeutics utilizing a biological tool known as CRISPR/Cas9, which stands for Clustered, Regularly Interspaced Short Palindromic Repeats (“CRISPR”)/CRISPR associated 9 (“Cas9”). This is a technology for genome editing, the process of altering selected sequences of genomic deoxyribonucleic acid (“DNA”). We believe that CRISPR/Cas9 technology has the potential to transform medicine by both producing therapeutics that permanently edit and/or correct disease-associated genes in the human body with a single treatment course, and creating enhanced engineered cells that can treat oncological and immunological diseases. Our combination of deep scientific, technical and clinical development experience, along with our intellectual property (“IP”) portfolio, puts us in a position to unlock broad therapeutic applications of the CRISPR/Cas9 technology and create new classes of therapeutic products.

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 these 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, 2019.

Our mission is to build a company to develop curative genome editing treatments that can positively transform the lives of people living with severe and life-threatening disease. 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 to help more patients;
- Foster an environment that is 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 CRISPR/Cas9 platform across two areas: *in vivo* applications, in which CRISPR/Cas9 is the therapy, delivered to target cells within the body; and *ex vivo* applications, in which CRISPR/Cas9 creates the therapy of engineered human cells. All of our revenue to date has been collaboration revenue. Since our inception and through September 30, 2020, we have raised an aggregate of approximately \$893.6 million to fund our operations, of which \$272.6 million was through our collaboration agreements, \$170.5 million was from our initial public offering and concurrent private placements, \$249.1 million was from follow-on offerings, \$116.4 million was from at-the-market offerings and \$85.0 million was from the sale of convertible preferred stock.

The breadth of our CRISPR/Cas9 platform and delivery technology allows us to pursue a multitude of therapeutic targets/clinical indications. Specifically, we can target diseases that have the potential to be addressed by directly editing specific genes (i.e., gene knockout, repair, or insertion) as well as diseases that may be targeted by genetically engineered cell therapies. The successful treatment of these disorders may require various types of genome edits, CRISPR/Cas9 elements and DNA templates. We have assembled multiple *in vivo* and engineered cell therapy capabilities into a pipeline that reflects our full-spectrum approach and leverages the modularity inherent in our platform.

Our diversified pipeline includes *in vivo* development programs targeting genetic diseases, including transthyretin amyloidosis (“ATTR”), hemophilia A and hemophilia B, which we are co-developing with Regeneron Pharmaceuticals, Inc. (“Regeneron”), and hereditary angioedema (“HAE”). Our pipeline also includes *ex vivo* programs consisting of two separate efforts: (i) a set of proprietary programs focused on engineered cell therapies to treat various cancers and autoimmune diseases including our lead *ex vivo* program to target Wilms’ Tumor 1 (“WT1”) for acute myeloid leukemia (“AML”); and (ii) partnered programs developed in collaboration with Novartis Institutes for BioMedical Research, Inc. (“Novartis”), focused on chimeric antigen receptor (“CAR”) T (“CAR-T”) cells, hematopoietic stem cells (“HSCs”), the stem cells from which all of the various types of blood cells originate, and stem cells in the eye, or ocular stem cells (“OSCs”).

Our Pipeline

Our diversified pipeline includes *in vivo* and *ex vivo* programs. Our *in vivo* programs focus on treating patients that have significant unmet medical needs due to diseases attributable to genes expressed in the liver – ATTR (which we are co-developing with Regeneron) and HAE. Delivery plays a key role in our *in vivo* therapeutic approach. We have shown in animal models that our proprietary lipid nanoparticle (“LNP”) delivery technology, which encapsulates the therapeutic Cas9 messenger RNA (“mRNA”) and guide RNA (“gRNA”) into LNPs, can systemically deliver these therapeutic components to the liver.

For *ex vivo* applications, our wholly owned programs focus on next-generation, engineered cell therapy solutions that utilize antigen-specific T cell receptors (“TCRs”). The cells to be modified *ex vivo* can come from the individual patient (autologous source) or from another individual (allogeneic source). Our goal for the *ex vivo* pipeline is to move from autologous to allogeneic therapies, and from liquid to solid tumors.

We believe our full spectrum approach to *in vivo* and *ex vivo* programs positions us to build a pipeline across a wide range of indications.

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 ATTR and HAE, using a knockout approach. Our current efforts on *in vivo* delivery focus on the use of LNPs for delivery of the CRISPR/Cas9 complex to the liver.

Transthyretin Amyloidosis – (“ATTR”)

ATTR 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 (“hATTR”). Over 120 different genetic mutations are currently known to cause hATTR.

Deposits of TTR amyloid in the heart, nerves and/or other tissues can lead to diverse disease manifestations, including two main hereditary forms – hATTR with polyneuropathy (“hATTR-PN”), and hATTR with cardiomyopathy (“hATTR-CM”). Typical onset of disease symptoms is during adulthood and can be fatal within 2 to 15 years. Estimates suggest that approximately 50,000 patients suffer from hATTR worldwide.

In addition to the hereditary forms described above, ATTR can also develop spontaneously in the absence of any *TTR* gene mutation. This wild-type ATTR (“wtATTR”) 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 wtATTR with cardiomyopathy (“wtATTR-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 also demonstrated the transient nature of our proprietary modular LNP delivery system, which was rapidly cleared from circulation, with all CRISPR/Cas9 complex undetectable in blood and liver within ten days of administration. Our lead candidate, NTLA-2001, applies an *in vivo* liver gene knockout approach for the treatment of ATTR. In October 2020, we announced the authorization of our Clinical Trial Application (“CTA”) by the United Kingdom’s Medicines and Healthcare products Regulatory Agency (“MHRA”) to initiate our Phase 1 study to evaluate NTLA-2001 for the treatment of hATTR-PN. Subject to the potential impact of the COVID-19 pandemic, we expect to dose the first patient in this Phase 1 trial during the fourth quarter of 2020. In addition, we are submitting additional regulatory applications to enable enrollment in other countries as part of our global clinical development plans. The Phase 1 study will be a two-part, open label, multi-center study in adults with hATTR-PN to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of NTLA-2001, which will include the measurement of serum TTR levels following a single intravenous infusion. NTLA-2001 is part of a co-development and co-promotion (“Co/Co”) agreement directed to our first collaboration target with Regeneron, ATTR (the “ATTR Co/Co”), for which we are the clinical and commercial Lead Party and Regeneron is the Participating Party (see Note 7 to the condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q for further detail). Pursuant to the ATTR Co/Co agreement, Regeneron funded approximately 50% of the program’s development costs through 2019. On December 13, 2019, Regeneron informed us that it would exercise its right under the ATTR Co/Co agreement to modify its share of worldwide development costs and profits from 50% to 25%, effective in mid-June 2020.

Hereditary Angioedema – (“HAE”)

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 most patients, though some patients still experience breakthrough attacks and such treatment options require regular injections which can be associated with significant treatment burden and impact on quality of life.

Using our modular LNP delivery system, we aim to knock out the *prekallikrein B1* (“*KLKB1*”) gene with a single course of treatment to reduce plasma kallikrein activity to prevent excess bradykinin production leading to HAE attacks. 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 a clinically effective approach as a prophylactic treatment for HAE.

On May 7, 2020, we announced a development candidate for the treatment of HAE, NTLA-2002, a wholly owned program. We have completed a NHP durability study of our lead LNP formulation in support of NTLA-2002, which resulted in a year-long therapeutically relevant reduction of serum kallikrein protein levels and activity following a single dose. In addition, during the third quarter of 2020 we have initiated Good Laboratory Practices (“GLP”) toxicology studies in preparation for an IND or IND-equivalent regulatory submission for NTLA-2002 in the second half of 2021.

Ex Vivo Programs

We are independently researching and developing proprietary engineered cell therapies to treat various oncological and autoimmune diseases, for example TCR-engineered 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 exploring non-CAR-T cellular approaches that use immune cells, including T cells expressing recombinant TCRs, for oncology indications. For example, in our existing collaboration with IRCCS Ospedale San Raffaele (“OSR”), a leading European research-university hospital, we have identified optimized TCRs that recognize a WT1 target that could be used to treat a variety of cancers.
- 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.
- We are also exploring methods to apply CRISPR/Cas9 editing to CD4 immune cells to induce a non-reverting regulatory T cell phenotype, to create therapies that address autoimmune diseases.

In addition, based on our collaboration and technology, Novartis is developing therapies using CAR-T cells for oncology indications, as well as HSC and OSC-based therapies for a variety of diseases.

Acute Myeloid Leukemia – (“AML”)

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 have been nearly 11,000 deaths due to AML, as well as over 21,000 new AML cases in the U.S. in 2019. While AML can occur at any age, the prevalence of the disease increases with age, resulting in a median age at diagnosis of 67 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.

We have nominated NTLA-5001 as our first engineered T cell therapy development candidate for the treatment of AML, utilizing our TCR-directed approach to target the WT1 intracellular antigen. Our WT1-directed TCR T-cell therapy aims to develop 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 endogenous TCR with a natural, high affinity therapeutic TCR. The resulting cells are engineered to be capable of specific and potent killing of AML blasts without bone marrow cell toxicity. In February 2020, we presented data demonstrating that the selection of a natural, high-affinity TCR, in combination with our CRISPR-enabled engineering and targeted insertion, results in an engineered T cell capable of specific and potent killing of primary AML blasts. Importantly, our studies showed that CRISPR-enabled engineering overcomes key challenges of traditional TCR approaches, such as mispairing between therapeutic and endogenous TCR, therefore creating a more homogenous T cell product. The cells engineered with our lead WT1 TCR also exhibited no detectable reactivity to bone marrow cells, which express WT1 at low levels. In May 2020, we presented data on our proprietary T cell engineering process in support of NTLA-5001. The data presented showed that our proprietary process enables multiple, highly efficient, sequential edits in T cells, whether knocking out or inserting genes. This technology yields engineered cells with high anti-tumor activity and favorable attributes, including a desired memory phenotype, which is associated with longer lasting treatment effects. Importantly, chromosomal translocations (i.e., undesired chromosomal rearrangements) were similar to background levels in untreated cells. We continue to advance IND-enabling activities and we are on track to submit an IND or IND-equivalent for NTLA-5001 in the first half of 2021.

Research Collaboration with Novartis

In December 2019, the research term under our collaboration agreement with Novartis ended, although the 2014 Novartis Agreement remains in effect. Accordingly, Novartis has selected various CAR-T cell, HSC and OSC targets for continued development, for which we will be eligible to receive milestone and royalty payments in the future. Further, we are eligible to earn up to \$230.3 million in development, regulatory and sales-based milestone payments and mid-single-digit royalties, in each case, on a per-product basis for the products developed by Novartis, subject to certain target-based limitations. During the first quarter of 2020, the U.S. Food and Drug Administration (“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 a \$5.0 million milestone payment that was previously constrained as collaboration revenue within the condensed consolidated statement of operations and comprehensive loss. Novartis is currently actively recruiting patients for its Phase 1/2 study of QTQ923 and HIX763, both candidates which were developed under the research collaboration. For more information regarding our collaboration with Novartis, see the section below entitled “Collaborations - Novartis.”

Other Research Programs

We are pursuing a number of *in vivo* and *ex vivo* genome editing programs. Within our *in vivo* research efforts, we continue to work on programs such as primary hyperoxaluria Type 1, alpha-1 antitrypsin deficiency, hemophilia A and hemophilia B which leverage our capabilities to knockout, insert and make consecutive edits to the genome. 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 also investigating delivery strategies that target tissues outside of the liver.

Within our *ex vivo* research efforts, 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. Further, we continue to advance efforts to move from autologous to allogeneic and from liquid to solid tumors. Our researchers are developing and improving cell-engineering manufacturing and delivery processes that, we believe, are designed to allow us to deliver T cell therapies with high levels of editing, achieve robust levels of expansion, ensure desirable memory phenotypes, improve function and reduce translocations. These platform advances will support NTLA-5001 and other ongoing research programs.

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 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 has been 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 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, 2020, excluding 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 and \$33.8 million primarily for research and development services 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, 2020, we have recognized \$116.7 million of collaboration revenue under all arrangements, including \$22.2 million and \$46.4 million during the three and nine months ended September 30, 2020 and \$5.8 million and \$17.8 million during the three and nine months ended September 30, 2019, respectively, in the condensed consolidated statements of operations and comprehensive loss. This includes \$1.2 million and \$9.8 million during the three and nine months ended September 30, 2020, respectively, and \$2.6 million and \$8.4 million during the three and nine months ended September 30, 2019, 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*. As of September 30, 2020 and December 31, 2019, we had accounts receivable of \$1.2 million and \$3.6 million, respectively, and deferred revenue of \$79.6 million and \$28.8 million, 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.

Through September 30, 2020, excluding amounts allocated to Novartis' purchase of the Company's Class A-1 and Class A-2 Preferred Units, we had recorded a total of \$62.4 million in cash under the 2014 Novartis Agreement and the Novartis Amendment. Through September 30, 2020, we have recognized \$62.4 million of collaboration revenue, including \$5.0 million related to a development milestone that was recognized in the first quarter of 2020 and \$4.8 million and \$14.3 million in the three and nine months ended September 30, 2019, respectively. No collaboration revenue was recorded during the three months ended September 30, 2020, related to the 2014 Novartis Agreement and the Novartis Amendment. As of September 30, 2020, we had no accounts receivable related to the 2014 Novartis Agreement and the Novartis Amendment. As of December 31, 2019, we had accounts receivable of \$1.0 million related to the 2014 Novartis Agreement and the Novartis Amendment. As of September 30, 2020 and December 31, 2019, we had no deferred revenue related to the 2014 Novartis Agreement and the Novartis Amendment.

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 with Novartis and Regeneron.

Research and Development

Research and development expenses consist of expenses incurred in performing research and development activities, including compensation and benefits, which includes equity-based compensation, for full-time research and development employees, allocated facility-related expenses, overhead expenses, clinical manufacturing costs, license and milestone fees, contract research 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 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, 2020 and 2019

The following table summarizes our results of operations for the three months ended September 30, 2020 and 2019:

	Three Months Ended September 30,		Period-to- Period Change
	2020	2019	
Collaboration revenue	\$ 22,220	\$ 10,616	\$ 11,604
Operating expenses:			
Research and development	39,756	27,513	12,243
General and administrative	10,566	8,431	2,135
Total operating expenses	50,322	35,944	14,378
Operating loss	(28,102)	(25,328)	(2,774)
Interest income	262	1,694	(1,432)
Net loss	\$ (27,840)	\$ (23,634)	\$ (4,206)

Collaboration Revenue

Collaboration revenue increased \$11.6 million to \$22.2 million during the three months ended September 30, 2020, as compared to \$10.6 million during the three months ended September 30, 2019. The increase in collaboration revenue during the three months ended September 30, 2020 is primarily due to the Company recording \$15.3 million related to the transfer of control of the license to develop the Factor VIII target for hemophilia A, partially offset by a decrease in revenue related to the Novartis collaboration. 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 \$12.2 million to \$39.8 million during the three months ended September 30, 2020, as compared to \$27.5 million during the three months ended September 30, 2019.

The following table summarizes our research and development expenses for the three months ended September 30, 2020 and 2019, 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
	2020	2019		
Pipeline and platform development expenses	\$ 21,274	\$ 13,866	\$ 7,408	53%
Employee-related expenses	10,968	8,033	2,935	37%
Allocated facility-related expenses	4,712	3,902	810	21%
Stock-based compensation expense	2,775	1,513	1,262	83%
Other expenses	27	199	(172)	-86%
Total research and development expenses	\$ 39,756	\$ 27,513	\$ 12,243	44%

The increase in research and development expenses for the three months ended September 30, 2020 compared to the three months ended September 30, 2019 was primarily attributable to:

- approximately \$7.4 million in increased pipeline and platform development expenses driven by increased costs as we prepared to enter the clinic for NTLA-2001, increased preclinical studies for NTLA-2002 and NTLA-5001, and an upfront payment associated with a research collaboration and licensing agreement;

- approximately \$2.9 million in employee-related expenses driven by an increase in the size of our workforce due to the advancement of our programs;
- approximately \$0.8 million in increased facility-related expenses primarily related to rent, depreciation and technology expense allocated to research and development; and
- approximately \$1.3 million in increased stock-based compensation driven by our larger workforce.

Through 2020, we expect research and development expenses to increase as we continue to grow our development team, execute clinical trials for ATTR and advance our AML and HAE programs towards clinical development.

General and Administrative

General and administrative expenses increased by approximately \$2.1 million to \$10.6 million during the three months ended September 30, 2020, compared to \$8.4 million during the three months ended September 30, 2019. This increase was primarily related to employee related expenses, including stock-based compensation, of \$2.0 million.

Interest Income

Interest income decreased by approximately \$1.4 million to \$0.3 million during the three months ended September 30, 2020 as compared to \$1.7 million during the three months ended September 30, 2019. This decrease was due to a decline in investment income due to market conditions.

Comparison of Nine Months Ended September 30, 2020 and 2019

The following table summarizes our results of operations for the nine months ended September 30, 2020 and 2019:

	<u>Nine Months Ended September 30,</u>		<u>Period-to-</u>
	<u>2020</u>	<u>2019</u>	<u>Period Change</u>
Collaboration revenue	\$ 51,399	\$ 32,167	\$ 19,232
Operating expenses:			
Research and development	112,177	76,682	35,495
General and administrative	33,406	32,082	1,324
Total operating expenses	<u>145,583</u>	<u>108,764</u>	<u>36,819</u>
Operating loss	(94,184)	(76,597)	(17,587)
Interest income	2,145	5,340	(3,195)
Net loss	<u>\$ (92,039)</u>	<u>\$ (71,257)</u>	<u>\$ (20,782)</u>

Collaboration Revenue

Collaboration revenue increased approximately \$19.2 million to \$51.4 million during the nine months ended September 30, 2020, as compared to \$32.2 million during the nine months ended September 30, 2019. The increase in collaboration revenue during the nine months ended September 30, 2020 is primarily caused by an \$8.4 million one-time cumulative catch-up adjustment related to the modification of the 2016 Regeneron Agreement as well as \$15.3 million recorded due to the transfer of control of the license to develop the Factor VIII target for hemophilia A, partially offset by a decrease in revenue related to the Novartis collaboration. 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 \$35.5 million to \$112.2 million during the nine months ended September 30, 2020, as compared to \$76.7 million during the nine months ended September 30, 2019.

The following table summarizes our research and development expenses for the nine months ended September 30, 2020 and 2019, together with the changes in those items in dollars (in thousands) and the respective percentages of change:

	<u>Nine Months Ended September 30,</u>		<u>Period-to- Period Change</u>	<u>Percent Change</u>
	<u>2020</u>	<u>2019</u>		
Pipeline and platform development expenses	\$ 57,168	\$ 34,927	\$ 22,241	64%
Employee-related expenses	31,932	23,052	8,880	39%
Allocated facility-related expenses	14,539	11,820	2,719	23%
Stock-based compensation expense	7,325	5,392	1,933	36%
Other expenses	1,213	1,491	(278)	-19%
Total research and development expenses	<u>\$ 112,177</u>	<u>\$ 76,682</u>	<u>\$ 35,495</u>	<u>46%</u>

The increase in research and development expenses for the nine months ended September 30, 2020 compared to the nine months ended September 30, 2019 was primarily attributable to:

- approximately \$22.2 million in increased pipeline and platform development expenses driven by increased manufacturing and related costs as we prepared to file our CTA and enter the clinic for NTLA-2001, increased preclinical studies for NTLA-2002 and NTLA-5001, and upfront payments associated with a research collaboration and licensing agreement;
- approximately \$8.9 million in employee-related expenses driven by an increase in the size of our workforce due to the advancement of our programs;
- approximately \$2.7 million in increased facility-related expenses primarily related to rent, depreciation and technology expense allocated to research and development; and
- approximately \$1.9 million in increased stock-based compensation driven by our larger workforce.

Through 2020, we expect research and development expenses to increase as we continue to grow our development team, execute clinical trials for ATTR and advance our AML and HAE programs towards clinical development.

General and Administrative

General and administrative expenses increased by approximately \$1.3 million to \$33.4 million during the nine months ended September 30, 2020, compared to \$32.1 million during the nine months ended September 30, 2019. This increase was primarily related to a \$3.2 million increase in employee-related expenses offset by a decrease in legal expenses of \$2.3 million.

Interest Income

Interest income decreased by approximately \$3.2 million to \$2.1 million during the nine months ended September 30, 2020 as compared to \$5.3 million during the nine months ended September 30, 2019. This decrease was due to a decline in investment income due to market conditions.

Liquidity and Capital Resources

Since our inception through September 30, 2020, we have raised an aggregate of \$893.6 million to fund our operations, of which \$272.6 million was through our collaboration agreements, \$170.5 million was from our initial public offering and concurrent private placements, \$249.1 million was from follow-on public offerings, \$116.4 million was from at-the-market offerings and \$85.0 million was from the sale of convertible preferred stock.

As of September 30, 2020, we had \$407.9 million in cash, cash equivalents and marketable securities.

We are entitled to receive research payments under our collaboration with Novartis and are also 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.

Follow-on Offering

On June 1, 2020, we entered into an underwriting agreement related to a public offering of 6,301,370 shares of our common stock, par value \$0.0001 per share, 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. The offering closed on June 5, 2020 and we received net proceeds of \$107.7 million, after deducting the underwriting discount, commissions and approximately \$0.4 million in offering expenses.

Shares Issued in Private Placement to Regeneron

As described in Note 7 to our condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q, in May 2020 we entered into the 2020 Regeneron Amendment. Simultaneously with the 2020 Regeneron Amendment, we and Regeneron entered into the 2020 Stock Purchase Agreement, under which we sold to Regeneron 925,218 shares of our common stock, par value \$0.0001 per share, for aggregate cash consideration of \$30.0 million, or \$32.42 per share, representing a 100% premium over the volume-weighted average trading price of our common stock during the 30-day period prior to the closing. Under the 2020 Stock Purchase Agreement, Regeneron will not dispose of any shares of common stock it beneficially owns in Intellia until the termination of the Technology Collaboration Term (see Note 7). After applying equity accounting guidance to measure the issuance of the shares, \$12.6 million was recorded as fair value in the condensed consolidated statement of stockholders' equity for the shares.

At-the-Market Offering Programs

In October 2018, we entered into an Open Market Sale Agreement (the "2018 Sales Agreement") with Jefferies LLC ("Jefferies"), under which Jefferies was able to offer and sell, from time to time in "at-the-market" offerings, shares of our common stock having aggregate gross proceeds of up to \$100.0 million. We paid to Jefferies cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2018 Sales Agreement. We issued 5,890,648 shares of our common stock at an average price of \$16.98 per share in accordance with the 2018 Sales Agreement for aggregate net proceeds of \$96.4 million, after payment of cash commissions to Jefferies and approximately \$0.6 million related to legal, accounting and other fees in connection with the sales. All shares related to the 2018 Sales Agreement had been sold as of December 31, 2019.

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 year ended December 31, 2019, we issued 287,231 shares of our common stock, in a series of sales, 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 Jefferies and approximately \$0.2 million related to legal, accounting and other fees in connection with the sales. During the nine months ended September 30, 2020, we issued 1,107,100 shares of our 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, 2020, \$130.0 million in shares of 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 2020, 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 begin clinical development.

Because our lead programs are still in the discovery, 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 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, 2020, as well as research and cost reimbursement funding from Regeneron, will enable us to fund our ongoing operating expenses and capital expenditure requirements at least through 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, 2020 and 2019:

	Nine Months Ended September 30,	
	2020	2019
	(In thousands)	
Net cash used in operating activities	\$ (9,686)	\$ (74,578)
Net cash used in investing activities	\$ (3,569)	\$ (2,708)
Net cash provided by financing activities	\$ 137,686	\$ 56,870

Net cash used in operating activities

Net cash used in operating activities of \$9.7 million during the nine months ended September 30, 2020 primarily reflects 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, offset in part by increased spend in our research and development activities. Net cash used in operating activities of \$74.6 million during the nine months ended September 30, 2019 primarily reflects increased spend in our research and development and general administrative activities, offset in part by the receipt of \$8.0 million and \$7.3 million in payments from our collaboration partners, Novartis and Regeneron, respectively, during those periods.

Net cash used in investing activities

During the nine months ended September 30, 2020 and 2019, our investing activities used net cash of \$3.6 million and \$2.7 million, respectively. The decrease in the nine months ended September 30, 2020 is primarily related 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. The decrease in the nine months ended September 30, 2019 is primarily related to the use of \$4.2 million in cash for the purchase of property and equipment, offset in part by an increase of \$1.5 million from marketable securities activity during the period, as \$265.5 million in marketable securities matured and \$264.0 million in marketable securities were purchased.

Net cash provided by financing activities

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. Net cash provided by financing activities of \$56.9 million during the nine months ended September 30, 2019 includes \$54.1 million in net proceeds from at-the-market offerings, \$2.2 million in cash received from the exercise of stock options and \$0.5 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, 2019.

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

In March 2020, we entered into a second amendment to the 130 Brookline Lease (the "Second Amendment"). The Second Amendment amends certain terms of our existing lease, dated October 21, 2014, as amended on April 5, 2019. The Second Amendment extends the term of the 130 Brookline Lease by approximately six years through January 31, 2031. This extended term is included as part of the lease liability and right-of-use asset at September 30, 2020. The Second Amendment also provides an option to extend the lease for two consecutive five-year terms. We recognized a right-of-use asset and lease liability of approximately \$7.3 million related to the Second Amendment.

In March 2020, we 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"). Our obligation to pay rent on the 281 Albany Lease will start on the date that is six months after the commencement date or the date on which we occupy 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. 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 will contribute an

aggregate of \$4.4 million toward the cost of construction and tenant improvements for the premises. We have the option to extend the 281 Albany Lease for two successive five-year terms.

There were no other material changes to our contractual obligations during the nine months ended September 30, 2020. 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, 2019.

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, 2020, we had cash equivalents and marketable securities of \$400.6 million consisting of interest-bearing money market accounts, commercial paper, asset-backed securities, corporate and financial institution debt securities and U.S. Treasury 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, 2020.

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, 2020.

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, 2020 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. As a result of the COVID-19 pandemic, since March 2020, we have requested that our employees work remotely, as appropriate. We have not identified any material changes in our internal control over financial reporting as a result of these changes to the working environment. We are continually monitoring and assessing the COVID-19 situation to determine any potential impacts on the design and operating effectiveness of our internal controls 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 3. Legal Proceedings” of our Annual Report on Form 10-K (“Annual Report”) for the fiscal year ended December 31, 2019 includes additional discussion of our current legal proceedings.

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, 2019 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 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.
- Clinical development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates.
- Results, including positive results, from our initial preclinical activities and 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 U.S. Food and Drug Administration (“FDA”) or any other regulatory agency. If we cannot replicate the 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.
- 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.
- Business interruptions resulting from the 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.
- 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.
- 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.
- *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.
- 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, 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 recent proceedings, as well as potential future proceedings, related to this patent family may affect our ability to utilize the 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.
- 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 the Discovery, Development, Manufacturing and Commercialization of Product Candidates

Risks Related to 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 the 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, which typically involves introducing a copy of a gene into a patient’s cells, and genome editing in recent years, *in vivo* CRISPR-based genome editing technologies are relatively new, and their therapeutic utility is largely unproven. In addition, even though cell therapy products have been developed and received regulatory approval in key jurisdictions, such as the United States (“U.S.”) and European Union (“EU”), no genome editing *in vivo* therapy or genome-edited engineered cell therapy has been approved, and the potential to successfully obtain approval remains unproven.

The CRISPR/Cas9 therapies, whether *in vivo* or engineered cell therapies, that we intend to develop have not yet been clinically tested by us, and we are not aware of any clinical trials for safety or efficacy having been completed by third parties involving these CRISPR/Cas9-based therapies. The scientific evidence to support the feasibility of developing *in vivo* products or engineered cell therapies based on the CRISPR/Cas9 technology is both preliminary and limited. 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 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.

We have principally concentrated our research efforts to date on bringing CRISPR/Cas9-based therapeutics to the clinic for various initial indications, and our future success is highly dependent on the successful development of CRISPR-based genome editing technologies, cellular delivery methods and therapeutic applications for these indications. These indications are the principal focus of our on-going development efforts, and 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 the U.S., state or 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. 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. It is impossible to predict when or if any of our programs will prove effective and safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of any of our future product candidates in humans. 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 applicable regulatory authorities would consider clinically meaningful, and a clinical trial can fail at any stage of testing. 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 marketing 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.

We may experience 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 future clinical trials that we could conduct, which could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- 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 at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations (“CROs”), the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of any product candidates may fail to show safety or efficacy, produce negative or inconclusive results and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon product development programs;
- the number of patients required for clinical trials of any product candidates may be larger than we anticipate, enrollment in these clinical trials may be lower than required by the regulatory agencies or slower than we anticipate, or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- regulatory agencies may require us to 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 contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants 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 clinical trials of our product candidates may be insufficient or inadequate, or not available in a reasonable timeframe;
- 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; and
- the FDA or other regulatory authorities may require us to submit additional data, such as long-term toxicology studies, or impose other requirements before permitting us to initiate or rely on a clinical trial.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our 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.

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

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 insertion of a gene sequence into a patient's chromosome 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 would have an adverse effect on our business, financial condition, 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 Sales, Marketing and Competition

Our ability to generate product revenue 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.

Our ability to generate product revenue is highly dependent on our ability to obtain regulatory approval of and successfully commercialize one or more of our product candidates. Our current product candidates and any other we discover 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, potency and efficacy of the product candidates in humans. We cannot be certain that we will be successful on any of these endeavors, or that any of our product candidates will be successful in clinical trials and, even if successful, that we will receive regulatory approval.

Our approach to developing therapies centers on using the 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. Because these are new therapeutic approaches, discovering, developing, manufacturing and commercializing our product candidates subject us to a number of challenges, including:

- obtaining regulatory clearance or approval to commence clinical trials in the U.S. from the FDA through an investigational new drug application (“IND”) or from other national regulatory agencies outside the U.S., such as the United Kingdom’s Medicines and Healthcare products Regulatory Agency (“MHRA”), 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;
- obtaining ethical clearance from the relevant IRBs and ethics committees to commence clinical trials in the U.S. and outside the U.S. because these agencies have very limited or no experience with gene editing generally, CRISPR/Cas9 in particular or therapeutics based on the same;
- obtaining regulatory approval for a BLA, or corresponding applications outside the U.S., such as a Marketing Authorization Application (“MAA”) from the United Kingdom (“UK”) 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;
- educating medical personnel, including clinical investigators, and patients regarding the potential benefits and side effect profile of each of our product candidates;
- developing processes for the safe administration of these products, including long-term follow-up for all patients who receive treatment with any of our product candidates;
- sourcing 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;
- establishing process development and manufacturing capabilities that can produce sufficient clinical and, if approved, commercial quantities of product candidates in accordance with the relevant FDA and other relevant regulatory agencies’ requirements;
- developing a manufacturing process and distribution network with a cost of goods that allows for an attractive return on investment; and
- establishing sales and marketing capabilities in anticipation of, and after obtaining, any regulatory approval to gain market authorization.

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 amyloidosis (“ATTR”), 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; and the FDA and other regulatory authorities have provided limited additional specific written guidance regarding preclinical or clinical studies or regulatory considerations for either *in vivo* or *ex vivo* therapeutics using genome editing technology. 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.

Also, uncertainty exists regarding the future scope and effect of the FDA’s application of its regulatory framework to CRISPR/Cas9 therapies, in particular relating to the review and approval of human therapeutic products because the current U.S. administration and federal legislators have publicly declared their intention to modify the current legal framework governing the FDA, as have candidates seeking federal executive and legislative positions in the U.S. in 2021. Any such changes to the FDA requirements could impact our ability to obtain approval for our products or sell them profitably. Also, upon completing its transition period as it exits the EU, the UK may enact legislation related to the approval and oversight of human therapeutics in that nation. Until any such legislation is enacted, we will be uncertain as to its effects on our business, including our ability to seek and obtain approval for our products in the UK.

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, including the genome editing field and engineered cell therapies, are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions.

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

- genome editing companies focused on CRISPR/Cas9 including: Beam Therapeutics Inc., Caribou Biosciences, Inc., CRISPR Therapeutics, Inc., Editas Medicine, Inc., ToolGen, Inc., Tracr Hematology Limited;
- other genome editing companies including: Allogene Therapeutics, Inc., bluebird bio, Inc., Collectis S.A., Homology Medicines, Inc., Poseida, Inc., Precision BioSciences, Inc. and Sangamo Therapeutics, Inc.; and
- gene therapy companies developing *in vivo* or *ex vivo* therapies, such as cell therapies, including: Asklepios Biopharmaceutical, Inc., bluebird bio, Inc., Collectis S.A., Gilead Sciences, Inc. (which acquired Kite Pharma, Inc.), Novartis A.G., Roche Holding AG (which acquired Spark Therapeutics, Inc.) and Voyager Therapeutics, Inc.

Our competitors 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.

To become and remain profitable, we must discover, develop, manufacture and eventually commercialize product candidates with significant market potential, which will require us to be successful in a range of challenging activities. These activities can include completing preclinical studies and clinical trials of product candidates, obtaining marketing approval for product candidates, manufacturing at a sufficient scale, marketing and selling products that are approved and satisfying any pre-approval, approval and post-marketing requirements. 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.

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. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if they are approved.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own 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, our product revenue or the profitability to us from these revenue streams is likely to be lower than if we were to market and sell any product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on 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 in collaboration with third parties, we may not be successful in commercializing our product candidates. Further, our business, results of operations, financial condition and prospects will be materially adversely affected.

Risks Related to the Industry

Results, including positive results, from our initial preclinical activities and 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 the 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.

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. Companies in the pharmaceutical and biotechnology industries have commonly suffered significant setbacks or delays in clinical studies after achieving positive results in early stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made before, during and after clinical studies were underway, or observations regarding the lack of safety or efficacy made in clinical studies, which could include new or previously unreported adverse events. In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in the relevant laws, regulations or regulatory policy during the period of product development.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in such studies nonetheless failed to obtain FDA or other necessary regulatory agency approval. If we fail to obtain results in our on-going, planned and future preclinical and clinical activities and studies sufficient to meet the requirements of the relevant regulatory agencies, the development timeline and regulatory approval and commercialization prospects for any potential product candidate, and, correspondingly, our business and financial prospects, would be materially adversely affected.

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”);
- 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.

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.

We may not be able to initiate or continue clinical trials for our current or future product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the U.S. If patients are unwilling to participate in our clinical studies because of concerns about, or negative publicity from, adverse events in the genome editing, gene therapy or engineered cell therapy fields, the novel nature of the CRISPR/Cas9 genome editing technology, the irreversibility of the effects of CRISPR/Cas9 or for other reasons, including competitive clinical studies for similar patient populations, then the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed. Other events, such as the COVID-19 pandemic, also could adversely impact the initiation, continuation and completion of our clinical trials by, for example, delaying the dosing of patients, or reducing the number of patients, healthcare providers or clinical facilities available or willing to participate in the clinical trials. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical studies altogether. In addition, any patients who would otherwise be eligible for clinical trials that we may hold may instead enroll in clinical trials of product candidates of our competitors.

Patient enrollment is affected by other factors including:

- the size, location and nature of the patient population;
- the severity of the disease under investigation;
- the patient eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the design of the clinical trial;
- the availability of alternative treatments;
- our payments for conducting clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in clinical trials may result in increased development costs for any of our potential future product candidates, which would cause our value to decline and limit our ability to obtain additional financing. Furthermore, we expect to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and, while we expect to enter into agreements governing their committed activities, we will have limited influence over their actual performance.

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.

Although we have selected our initial product candidates for clinical development for our ATTR, acute myeloid leukemia and hereditary angioedema programs, and commenced clinical trials in relation to NTLA-2001 for ATTR, we are at an early stage of development and our technology and approach has not yet led, and may never lead, to any product candidate deemed appropriate for clinical development by a regulatory agency or any approved or commercially successful products. 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 prone 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 adequate efficacy or an acceptable safety profile, gain regulatory approval, or become commercially viable.

We cannot provide any assurance that we will be able to successfully advance any product candidates that we discover through the research process. Our research programs may initially show promise, yet fail to yield product candidates for clinical development or commercialization for many reasons, including the following:

- our technology and approach may not be successful in identifying product candidates deemed appropriate for clinical development and commercialization;
- we may not be able or willing to assemble sufficient resources to acquire or discover product candidates for clinical development and commercialization;
- animal or other non-human models for the targeted disease may not be appropriate or available to conduct preclinical testing;
- testing in preclinical models may not be predictive of human clinical testing results because species have distinct genomic sequences that may require the use of species-specific guides and reagents;
- our product candidates may not succeed in preclinical or clinical testing;
- our planned risk mitigation strategy for selecting our initial indications may fail or we may not be able to efficiently apply learnings from our initial development programs to future development programs;
- progress made in one target or using one editing approach may not translate to any other target or editing approach;
- we may be unable to optimize the therapeutic efficiency, specificity, or selectivity of our future product candidates;
- our therapeutic delivery systems may fail so that even a product candidate with therapeutic activity might not demonstrate a clinically meaningful therapeutic effect;
- a product candidate may not demonstrate in patients the biological, chemical and pharmacological properties identified in laboratory and preclinical studies, or they may interact with human biological systems in unforeseen, ineffective or even harmful ways;
- a product candidate may on further study not replicate the results from earlier studies or be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- the therapeutic effect of a product candidate may not be permanent and may diminish over time;
- we may not be able to sufficiently control the effect of a product candidate to gain regulatory approval;
- a single treatment course may not be sufficient for a cure or therapeutic benefit, and it may take several treatment courses for the product to be effective;
- our product candidates may not be sufficiently well-tolerated for either one-time or repeat treatments necessary for maximum effectiveness;

- a well-defined and achievable pathway to regulatory approval may never materialize for a specific product candidate;
- competitors may develop alternatives that render our product candidates obsolete, redundant or less attractive;
- product candidates we develop may be covered by third-party or other exclusive rights or may not receive desired regulatory exclusivity, and we may be unable to maintain, expand or protect our intellectual property rights;
- the market for a product candidate may change during our program so that the continued development of that product candidate is no longer reasonable;
- we may be unable to manufacture the product candidates after transferring our manufacturing processes from our research and development facilities to larger-scale facilities operated by either a contract manufacturing organization (“CMO”) or by us, as well as delays or failure by our CMOs or us, including as a result of the COVID-19 pandemic, to make any changes to such manufacturing process to meet specifications for the product candidates’ specifications;
- a product candidate may not be capable of being produced in clinical and, if approved, commercial quantities at an acceptable cost, or at all;
- we may be unable to successfully maintain existing collaborations or licensing arrangements or enter into new ones throughout the development process as appropriate; and
- a product candidate may not be accepted as safe and effective by physicians, patients, hospitals, third-party payors and others in the medical community.

If any of these events occur, we may be forced to abandon our development efforts for a product candidate, program or programs, or we may not be able to identify, discover, develop, manufacture or commercialize product candidates, which would have a material adverse effect on our business and could potentially cause us to cease operations.

Because we have limited financial and managerial resources, we are initially focused on specific research programs. As a result, we may fail to capitalize on other viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases that may later prove to have greater commercial potential, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights. For additional information regarding the factors that will affect our ability to achieve revenue from product sales, see the risk factor entitled “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.”

If we do not successfully develop, manufacture and commercialize product candidates based upon our approach, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price. Further, our current focus on CRISPR/Cas9 technology for developing products as opposed to multiple, more proven technologies for product development increases the risk associated with our business. If we are not successful in developing a product candidate using CRISPR/Cas9 technology, we may not be able to successfully implement an alternative product development strategy.

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 as a framework for developing genome editing-based therapies is a recent development and may not become broadly accepted by physicians, patients, hospitals, third-party payors and others in the medical community. 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 physicians and medical centers capable of delivering any therapies that we develop;
- the willingness of patients 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. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products, particularly gene editing and engineered cell products. Coverage may be more limited than the purposes for which a therapeutic is approved by the FDA or comparable regulatory authorities in other jurisdictions. In addition, because our product candidates represent new approaches to the treatment of genetic-based diseases, we cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop.

In the U.S. and some other jurisdictions, patients who are provided medical treatment for their conditions 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 UK, that evaluate the use and cost-effectiveness of therapies, which impact the utilization and price of the medicine in such jurisdiction.

Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor’s determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

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 government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to maintain pricing sufficient to achieve or sustain profitability or may require co-payments that patients find unacceptably high. 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. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. Because our product candidates may have a higher cost of goods than conventional therapies, and may require long-term follow up evaluations, the risk that coverage and reimbursement rates may be inadequate for us to achieve profitability may be greater. There is significant uncertainty related to insurance coverage and reimbursement of newly approved products. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Moreover, increasing efforts by governmental and third-party payors in and outside the U.S. to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes.

We intend to seek approval to market our product candidates in different jurisdictions, which could include the U.S. and other selected foreign jurisdictions, such as the UK, certain EU members, China, Japan, Mexico, Brazil, Colombia, Argentina, Canada and Australia. If we obtain approval in any of these jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some markets, such as, for example, in the EU and the UK, the pricing of pharmaceutical products, including biologics, is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future health care reform measures.

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

In June 2016, a majority of the eligible members of the electorate in the UK voted to withdraw from the EU in a national referendum, commonly referred to as “Brexit.” Subsequently, the UK and the EU agreed to a withdrawal agreement (the “Withdrawal Agreement”). The Withdrawal Agreement was approved by the UK Parliament and the UK formally left the EU on January 31, 2020. Under the Withdrawal Agreement, the UK is subject to a transition period until December 31, 2020 (the “Transition Period”), during which EU rules will continue to apply. Negotiations between the UK and the EU are on-going and are expected to continue in relation to the customs and trading relationship between the UK and the EU following the expiry of the Transition Period.

The uncertainty concerning the UK’s legal, political and economic relationship with the EU after the Transition Period may 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).

Since the regulatory framework for pharmaceutical products in the UK covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime that applies to drugs and the approval of drug candidates in the UK. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the UK. Given the lack of comparable precedent, it is unclear what financial, trade and legal implications the withdrawal of the UK from the EU, especially in the case of the UK leaving the EU without an agreement defining their respective trading rights and obligations, would have and how such withdrawal would affect us. The long-term impact of Brexit, including on our business and our industry, will depend on the terms that are negotiated in relation to the UK’s future relationship with the EU, and we are closely monitoring the Brexit developments in order to determine, quantify and proactively address changes as they become clear.

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.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the U.S., our operations may be directly, or indirectly through our future, potential customers and third-party payors, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act (“FCA”), and data privacy and physician sunshine laws and regulations. These laws or their relevant foreign counterparts may impact, among other things, our proposed sales, marketing, and education programs and our relationships with healthcare providers, physicians and other parties through which we market, sell and distribute our products for which we obtain marketing approval. In addition, we may be subject to patient privacy regulation by the federal government and the states in the U.S. as well as other jurisdictions. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, individuals or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order, arrangement for or recommendation of the purchase, lease, order, arrangement for any good, facility, item or service, for which payment may be made, in whole or in part, 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. In addition, the Affordable Care Act (“ACA”) provides that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal FCA. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. 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, without limitation, the federal FCA, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from the federal government, including Medicare, Medicaid and other government payors, that are false or fraudulent or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims by, for example, promoting a product off-label. The FCA also permits a private individual acting as a “whistleblower” to bring civil whistleblower or *qui tam* actions against individuals (including biopharmaceutical manufacturers and sellers) on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. These laws impose criminal and civil penalties on violators;
- the federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) and its implementing regulations, which impose criminal and civil liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, 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. HIPAA violations can lead to civil and criminal liability;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (“HITECH”), and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions. In addition, state and non-U.S. laws govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effective requirements, thus complicating compliance efforts to comply with their respective provisions;
- 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 drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program (with certain exceptions) to report annually to the CMS, information related to payments or other transfers of value 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 physicians, other healthcare providers, and their immediate family members. Failure to submit required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately, and completely reported in an annual submission. 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 such as physician assistants and nurse practitioners;
- the Foreign Corrupt Practices Act (“FCPA”) and other laws which prohibit improper payments or offers of payments to foreign governments and their officials and political parties by U.S. persons and issuers as defined by the statute for the purpose of obtaining or retaining business. In the UK, for example, the UK Bribery Act 2010 prohibits the giving of financial or other advantages to encourage persons to perform their functions improperly, and does not include an exemption for facilitation payments;
- the Federal Food, Drug and Cosmetic Act, which prohibits, among other things, the commercialization of adulterated or misbranded drugs and medical devices and the Public Health Service Act, which prohibits, among other things, the commercialization of biological products unless a biologics license is in effect; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which 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; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

Because of the breadth of these laws and the limited statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring business arrangements comply with applicable healthcare 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 the business.

Various laws regulate the collection and use of personal data in relevant jurisdictions outside the U.S., such as the General Data Protection Regulation ("GDPR") in the EU and European Economic Area ("EEA"), related data protection and privacy laws of the EU and EEA member states, and the UK's Data Protection Act 2018 (such laws being described as "European Data Protection Law"), such as the European Data Protection Law. The European Data Protection Law applies to any business, regardless of its location, that provides goods or services to individuals in the EU or UK and, thus, could apply to our data processing activities that involve the personal data of individuals in EU member states or the UK. The European Data Protection Law imposes strict requirements on controllers and processors of personal data, including special protections for "sensitive information," which includes health and genetic information of individuals in the EU or the UK, expanded disclosures about how personal data is to be used, limitations on retention of information, mandatory data breach notification requirements and additional obligations when we contract with third-party processors in connection with the processing of the personal data. The European Data Protection Law grants individuals the right to object to the processing of their personal data, a strengthened right to request deletion of personal data in certain circumstances and other rights for individual data subjects. Further, the European Data Protection Law imposes strict rules on the transfer of personal data out of the EU or the UK to regions that have not been deemed to offer "adequate" privacy protections, such as the U.S. and other third countries. In addition, the European Data Protection Law provides that EU member states or the UK may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data. Failure to comply with the requirements of the European Data Protection Law may result in warning letters, mandatory audits, orders to cease/change our 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 claim damages resulting from infringement of the European Data Protection Law. The European Data Protection Law further grants non-profit organizations the right to bring claims on behalf of data subjects. The costs associated with ensuring compliance with the European Data Protection Law may be onerous and adversely affect our business, financial condition, results of operations and prospects. We may also need to rely on multiple third parties to comply with the European Data Protection Law, which could result in additional liability for us if they do not comply.

In addition, further to the UK's exit from the EU on January 31, 2020, often referred to as Brexit, the GDPR will continue to apply in the UK until the end of the transition period on December 31, 2020. Unless the transitional period is extended, as of January 1, 2021 the GDPR will be brought into UK law as the "UK GDPR", but there may be further developments about the regulation of particular issues such as UK-EU data transfers. We may be required to take steps to ensure the lawfulness of our data transfers, particularly if by the end of the transition period there will not be an EU Commission's adequacy decision regarding the UK.

On June 28, 2018, the State of California enacted the California Consumer Privacy Act of 2018 (“CCPA”), which became effective on January 1, 2020. The CCPA creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on covered entities (“businesses”) handling personal information of consumers or households. The CCPA requires covered businesses to provide certain disclosures to consumers about their data collection, use and sharing practices, and to provide California residents with expanded rights to access and delete their personal information and ways to opt-out of certain sales or transfers of their personal information. The CCPA became enforceable by the California Attorney General on July 1, 2020. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that may increase data breach litigation. The CCPA may have a significant impact on our handling of personal information and existing privacy policies and procedures. The uncertainty surrounding the integration of CCPA exemplifies the vulnerability of our business to the evolving regulatory environment related to personal information and protected health information.

In addition, while the CCPA has been receiving a lot of attention, other U.S. states have enacted and/or are considering laws that impose stringent privacy and/or data security requirements. Addressing these diverse requirements 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 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. Activities conducted in jurisdictions outside of the U.S. create the risk of unauthorized payments or offers of payments that are prohibited under the FCPA or comparable laws and regulations. It is our policy to implement safeguards to discourage these practices by our employees. 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.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations as well as other domestic and foreign legal requirements will involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. 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 civil, criminal and administrative penalties, damages, disgorgement, monetary fines, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other U.S. federal healthcare programs, 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 other 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 cause a pharmaceutical manufacturer to incur significant legal expenses and divert management’s attention from the operation of the business. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way. In addition, the approval and commercialization of any of our product candidates outside the U.S. will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

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 foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) additional regulation or restrictions on pricing and reimbursement; (iv) changes to private or governmental insurance practices; (v) the recall or discontinuation of our products; or (vi) additional record-keeping requirements. 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 foreign 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 current administration and federal legislators, as well as candidates seeking federal executive and legislative offices in the November 2020 elections in the U.S., have publicly declared their intention to significantly modify the current legal and regulatory framework for the health care system but details have not been agreed upon or disclosed.

Current legislation at the U.S. federal and state levels seeks to reduce healthcare costs and improve the quality of healthcare. In March 2010, 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”), was enacted, which substantially changed the way health care is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical and biotechnology industry. The Affordable Care Act, among other things, subjects biologic products to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extends the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjects manufacturers to new annual fees and taxes for certain branded prescription drugs and biologic agents, creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, effective as of January 1, 2019) point-of-sale discounts off negotiated prices of applicable 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 provides 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.

Some of the provisions of the Affordable Care Act have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, as well as recent efforts by the current administration to repeal or replace certain aspects of the Affordable Care Act. Since January 2017, the U.S. president has signed several executive orders and other directives designed to delay the implementation of certain provisions of the Affordable Care Act. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the Affordable Care Act. Further, significant uncertainty exists regarding the future scope and effect of the Affordable Care Act because the current administration and federal legislators have publicly declared their intention to significantly modify or repeal the legislation, and there are conflicting judicial decisions regarding the constitutionality of the law which is under review by the U.S. Supreme Court. We cannot predict the ultimate form or timing of any modification to, or repeal of, the Affordable Care Act or the effect that such modification or repeal would have on our business. Public announcements by the U.S. administration and members of the U.S. Congress have emphasized the administration’s significant interest in pursuing healthcare reform. Such reform efforts and any resulting changes to the Affordable Care Act, or related regulations and laws, could impact our ability to sell our products profitably.

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”), the Medicare sequester reductions under the Budget Control Act of 2011 have been suspended from May 1, 2020 through December 31, 2020 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. In December 2017, the U.S. president signed into law the Tax Cuts and Jobs Act (“TCJA”) which, among other things, repealed the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year (the “individual mandate”), effective January 1, 2019. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseparable feature of the Affordable Care Act, and therefore, because it was repealed as part of the TCJA, the remaining provisions of the Affordable

Care Act are invalid as well. The current Administration and CMS have both stated that the ruling will have no immediate effect, and 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 Affordable Care Act. The State of California and the other plaintiffs in this case asked the U.S. Supreme Court for authorization to appeal the decision of the Fifth Circuit. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review this case and allotted one hour and 20 minutes for oral arguments, which is scheduled to occur on November 10, 2020. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results. We will continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business. These laws may result in additional reductions in Medicare, Medicaid and other healthcare funding, or insured patients generally, which could have a material adverse effect on our future, potential customers and, accordingly, our financial operations.

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 the current administration and federal legislators have publicly declared 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.

The continuing efforts of governments, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls could harm our business, financial conditions and prospects and may adversely affect:

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

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for any approved product. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability or commercialize our product candidates, if approved.

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 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; disruption in utility services; human error; insufficient personnel; inability to meet legal or regulatory requirements; or disruptions in the operations of our suppliers.

Our product candidates that are regulated as biologics, will require processing steps that are more complex than those required for 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. Accordingly, we will employ multiple steps to control the manufacturing process to ensure that the process works and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process,

could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims and litigation, insufficient inventory or production interruption. 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 specifications with consistent and acceptable production yields and costs.

In addition, the FDA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA or other foreign regulatory authorities may require that we not distribute a lot until the relevant agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures, product recalls or production interruption. Lot failures, product recalls or production interruption could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects. Problems in our manufacturing process could restrict our ability to meet market demand for our products.

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. 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 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 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 UK'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.

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 sometime after we have received regulatory approval for the commercial sale of a product candidate that we discover. 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;
- completing research, preclinical and clinical development of 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, including establishing and maintaining commercially viable supply relationships with third parties, such as CMOs, and potentially establishing our own manufacturing capabilities and infrastructure;
- 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. Our expenses could increase beyond expectations if we are required by the FDA or other regulatory agencies, domestic or foreign, to change our manufacturing processes or assays, or to perform clinical, nonclinical or other types of additional studies. If we are successful in obtaining regulatory approvals to market one or more product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price and whether we own the commercial rights for that territory. If the number of our addressable disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. 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. Our operations to date have been limited to organizing and staffing our company, business and scientific planning, raising capital, acquiring and developing technology, identifying potential product candidates, undertaking research and early preclinical studies of potential product candidates for ourselves and collaborators, developing the necessary manufacturing capabilities and evaluating a clinical path for our pipeline programs. All of our product candidates are still in the preclinical development or clinical stage. We have not yet demonstrated our ability to successfully initiate or execute 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 \$92.0 million for the nine months ended September 30, 2020. As of September 30, 2020, we had an accumulated deficit of \$392.9 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, as amended (the “2014 Novartis Agreement”) regarding the discovery of new CRISPR/Cas9-based therapies principally using chimeric antigen receptor T (“CAR-T”) cells and hematopoietic stem cells (“HSCs”). Under the Novartis collaboration agreement, we received a commitment to advance multiple programs. Pursuant to the 2014 Novartis Agreement, we granted Novartis exclusive rights to further develop and commercialize products arising out of the CAR-T cell program during the research term. Regarding HSCs, we are jointly advancing multiple programs with Novartis and have agreed to a process for assigning development and ownership rights, which may enable us to develop our own proprietary HSC pipeline. In December 2018, we expanded our collaboration agreement with Novartis to include discovery of CRISPR/Cas9-based therapies using certain limbal stem cells primarily against selected gene targets by Novartis. The research portion of our agreement with Novartis ended in December 2019, and we cannot guarantee that Novartis will continue to pursue programs that it has selected through our collaboration.

In April 2016, we entered into a collaboration agreement with Regeneron, which we amended in May 2020. The collaboration agreement, as amended, 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, pursuant to which we and Regeneron 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. Pursuant to the Regeneron collaboration agreement, as amended, we granted Regeneron exclusive rights to select up to 15 initial targets, subject to certain restrictions and modifications. We have retained the rights to solely develop certain indications. Other indications, such as ATTR, are subject to co-development and co-promotion (“Co/Co”) agreements with Regeneron. We also have the right to choose additional liver targets for our own development during the collaboration term, which may be subject to additional Co/Co options by Regeneron. In July 2018, we entered into the first Co/Co agreement directed to ATTR (the “ATTR Co/Co”), under which we are the clinical and commercial lead for ATTR activities. On December 13, 2019, Regeneron informed us that it would exercise its right under the ATTR Co/Co agreement to modify its share of worldwide development costs and profits from 50% to 25%, beginning in mid-June 2020. We continue to lead the development and commercialization of any resulting ATTR products. 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 such activities. Under the Hemophilia Co-Co agreements, worldwide development costs and profits of any future 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 under collaboration 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 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 in the applicable territories, or if either of our collaboration partners 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 therapeutic-focused collaborations provide us with important technologies and/or funding for our programs and technology, and we expect to receive additional technologies and funding under these and other collaborations in the future. Our existing therapeutic collaborations, and any future collaborations we enter into, may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply;
- collaborators may not perform their obligations as expected;
- collaborators may dispute the amounts of payments owed;
- collaborators 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 the collaborators' strategic focus or available funding, or external factors, such as a strategic transaction that may divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could develop independently, or with third parties, products that compete directly or indirectly with our products and product candidates if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators 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;
- collaborators may dispute ownership or rights in jointly developed technologies or intellectual property;
- collaborators may fail to comply with applicable legal and regulatory requirements regarding the development, manufacture, sale, distribution or marketing of a product candidate or product;
- collaborators with sales, marketing, manufacturing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the sale, marketing, manufacturing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation, payment obligations or the preferred course of discovery, development, sales or marketing, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional and burdensome responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators 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;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- if a collaborator of ours is involved in a business combination or cessation, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us; and
- collaborations may be terminated by the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates, or potentially 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 one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development and commercialization of our technology and product candidates could be delayed and we may need additional resources to develop product candidates and our technology. 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.

For some of our programs, we may in the future determine to collaborate with pharmaceutical and biotechnology companies for discovery, development and potential commercialization of 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. 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 discovery efforts or the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential manufacture or commercialization, or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to 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.

Risks Related to Our Reliance on Third Parties

We expect 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 for our product candidates. We will make changes as we work to optimize the manufacturing process, and we 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 pursuant to inspections that will be conducted after we submit an application to the FDA or other relevant foreign regulatory agencies. We will be dependent on our CMO partners to 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 legal and regulatory requirements for manufacture, including current good manufacturing practice ("cGMP"), and in certain cases, current good tissue practice ("cGTP"), requirements of our product candidates. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of, as applicable, the FDA or other regulatory authorities, they will not be able to secure and/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 a comparable foreign regulatory authority, as applicable, does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

Events such as the 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. Additionally, these events could also impact the regulatory agencies' ability to inspect and approve our vendors, including CMOs, within our currently expected timeframe.

We will rely on third parties to conduct our 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 will 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 will rely heavily on third parties over the course of our 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") requirements, which are regulations and guidelines enforced by the FDA, EU 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 FDA or comparable foreign 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 failure or any failure by these third parties to comply with these requirements or to recruit a sufficient number of patients may require us to repeat 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 UK 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 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 do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure 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 could divert healthcare resources away from our clinical trial sites to focus on pandemic concerns, including adversely impacting the availability of necessary materials and clinical trial personnel. 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.

The COVID-19 pandemic and government measures taken in response 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 our 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 to experience 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 are submitted for or receive marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources, the significant competition for qualified 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 to otherwise effectively manage the expansion of our operations. The expansion of our operations may lead to significant costs, and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business and development plans or disrupt our operations.

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 Leibold, our Executive Vice President and Chief Medical Officer, José E. Rivera, our Executive Vice President and General Counsel, Andrew Schiermeier, our Executive Vice President and Chief Operating Officer and Laura Sepp-Lorenzino, our Executive Vice President and Chief Scientific Officer as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment arrangements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be important for our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products using our technology. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies, universities and research institutions for similar personnel. The market for qualified personnel in the biotechnology space generally, and genome editing and gene therapy fields in particular, in and around the Cambridge, Massachusetts area is especially competitive. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Further, some of the qualified personnel that we hire and recruit are not U.S. citizens, and there is uncertainty with regard to their future employment status due to the current U.S. administration’s announced intention of modifying the legal framework for non-U.S. citizens to be employed in the U.S. 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 have not previously submitted a BLA to the FDA, or similar approval filings to comparable foreign authorities, such as an MAA in the UK or EU. A BLA, an MAA or similar approval filings must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe and effective or, for biological products, safe, pure and potent for each desired indication. The application must also include significant information regarding the chemistry, manufacturing and controls for the product, and the manufacturing facilities must complete a successful pre-approval inspection by the FDA, or otherwise applicable foreign authority, prior to the approval or licensure of the product. We expect the novel nature of our product candidates to create further challenges in obtaining regulatory approval. For example, in the U.S., the FDA has not approved any nuclease edited cell therapies 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 opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain approval of any product candidates that we develop based on the completed clinical trials. Moreover, while we are not aware of any specific genetic or biomarker diagnostic tests for which regulatory approval would be necessary in order to advance any of our product candidates to clinical trials or potential commercialization, in the future regulatory agencies may 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. In March 2019, the WHO Expert Advisory Committee recommended initiating the first phase of a new global 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. Registration of these clinical trials in the WHO's registry is voluntary. 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 addition, clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- obtaining and maintaining regulatory authorization to conduct a trial, if applicable;
- the availability of financial resources to begin and complete the planned trials;
- reaching agreement on acceptable terms with prospective CROs, clinical trial sites and clinical investigators, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining approval at each clinical trial site by an independent IRB or relevant ethics committee;
- recruiting suitable patients to participate in a trial in a timely manner;
- having patients complete a trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol, not complying with GCP requirements or dropping out of a trial;
- addressing any patient safety concerns that arise during the course of a trial;

- addressing any conflicts with new or existing laws or regulations;
- adding new clinical trial sites; or
- manufacturing qualified materials under cGMP regulations for use in clinical trials.

Patient enrollment is a significant factor in the timing of clinical trials and is affected by many factors, including willingness of physicians to use a new therapy, the availability of existing treatments, and the geographic location of the trial. In addition, even if the regulatory authority accepts our CTA, the IRB or another ethics committee (whether local or national) may delay our ability to enroll and dose patients. Further, a clinical trial may be suspended or terminated by us, the IRBs for the institutions in which such trials are being conducted, another ethics committee, the DSMB for such trial 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, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product 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 grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions, must also authorize the manufacturing, marketing and sale of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative 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 approved for sale 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 regulatory requirements in international markets or to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Risks Related to the COVID-19 Pandemic

Business interruptions resulting from the COVID-19 outbreak or similar public health crises could 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. In December 2019, a novel strain of a virus named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), or coronavirus, which causes COVID-19, surfaced in Wuhan, China and has reached most of the world, including Cambridge, Massachusetts where our primary office and laboratory space is located. The 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. for certain countries and regions, 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, execution of our clinical trial for NTLA-2001 for ATTR, as well as timely completion of preclinical activities and initiation of planned clinical trials for other product candidates, 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 the planned initiation of our 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;
- limitations on travel that could interrupt key preclinical activities and trial activities, such as 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;
- interruption or delays in the operations of the FDA, MHRA and comparable foreign regulatory agencies, which may impact review, inspection, clearance 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 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 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 will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, distribution, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety and efficacy data, and other post-market information, 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. 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 may also require a REMS 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 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. The regulatory agencies in other jurisdictions could take similar action for noncompliance with their respective requirements and standards. 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 the market or voluntary or mandatory product recalls;
- 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. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. 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 policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the U.S. or abroad. For example, in the U.S., certain policies of the current or future U.S. administration may impact our business and industry. Namely, the current administration has taken, or may take, several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking and issuance of guidance. It is difficult to predict how any of these rules or requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory and legal compliance, we may lose any marketing approval that we may have obtained and we may not 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 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. 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 HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

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 UK, and our current and future requests for approval to conduct clinical trials in the UK 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 UK in connection with EU or UK clinical trials. As discussed above, the GDPR regulates the processing of personal data of data subjects in the EU or the UK 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 UK, 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.

Because we are conducting a clinical trial in the UK, and intend to conduct clinical trials in other jurisdictions outside the U.S., we must also ensure that we maintain adequate safeguards to enable the transfer of personal data outside of the relevant jurisdiction, in particular to the U.S., in compliance with the relevant data protection laws. We expect that we will continue to face uncertainty as to whether our efforts to comply with our obligations under the GDPR will be sufficient. 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 do not 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. In varying degrees and scope, national, state and local laws prohibit unfavorable or unfair treatment in the workplace of employees or candidates based on their age, gender, race, national origin, religion, disability or sexual orientation. Disability laws also expand upon the employment rights of veterans and persons with disabilities. At a federal level, Title VII of the Civil Rights Act of 1964 prohibit discrimination on the basis of race, color, religion, sex or national origin. The Fair Labor Standards Act establishes a national minimum wage, guarantees "time-and-a-half" for overtime in certain jobs, and prohibits oppressive employment of minors. The Americans with Disabilities Act, as amended, prohibits discrimination based on disability.

The Commonwealth of Massachusetts also has laws that expand on these 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 Our Intellectual Property

Risks Related to 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. 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. We cannot guarantee that our technology, 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. 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 is violating 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 the scope of our field of use under the license rights granted to us 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 pursuant to 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 (the “Caribou Award”). The panel instructed the parties to negotiate the terms of the Caribou Award, including Caribou’s future payments to us for the same.

On February 6, 2020, after considering additional submissions from the parties, the panel clarified that the Caribou Award is limited to a particular ongoing Caribou program, which seeks to develop a CAR-T cell product directed at CD19. The panel instructed the parties to seek to negotiate terms based on this scope. Accordingly, the Caribou Award will be subject to terms, including Caribou’s future payments to us to be negotiated by the parties or, if unsuccessful, adjudicated in additional arbitration or judicial proceedings.

Pursuant to the September 2019 interim award, the Caribou Award by the panel does not include the structural guide modifications intellectual property at issue in the arbitration, any other intellectual property exclusively licensed or sublicensed by Caribou to us under the Caribou License (including but not limited to the foundational CRISPR/Cas9 intellectual property co-owned by University of California, University of Vienna and Dr. Emmanuelle Charpentier), or any other of our intellectual property.

Upon, and subject to the terms of, a final award, which will follow further arbitration or legal proceedings, Caribou could be able to use the modified guide RNAs at issue for CAR-T cell human therapeutics directed at CD19. Either we or Caribou may challenge the arbitration panel’s decisions under limited circumstances. The additional time and legal costs associated with negotiating or arbitrating the terms of the Caribou Award, as well as its final terms, could adversely impact our exclusive right to use the particular modified guide RNAs in dispute and enable Caribou’s ability to compete with us (or our licensees) in the development of CAR-T cell human therapeutics directed at CD19, each of which may adversely affect our business.

In addition, 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. 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, 2020, 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. If it were to succeed in the interference, the Broad could seek to assert its issued patents against us based on our CRISPR/Cas9-based activities, including commercialization. Defense of these 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.

In addition, other third parties, such as Vilnius University, ToolGen, Inc., MilliporeSigma (a subsidiary of Merck KGaA) 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 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.

Third parties could also assert patent rights against us to seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize product candidates. For example, the Broad Institute or other third-parties that own issued patents, including patents claiming aspects of the CRISPR/Cas9 technology, could seek to assert such patents against us claiming that our activities, including those relating to the CRISPR/Cas9 technology, infringe their respective patents. Defense of these or similar claims, regardless of their merit, would involve substantial legal 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 any adjudicated 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 may be unable to further develop and commercialize our product candidates, which could harm our business significantly.

Third parties asserting their patent rights against us may seek and obtain injunctive or other equitable relief, which could effectively limit or block our ability to further develop and commercialize our product candidates. If we are found to infringe a third-party's valid intellectual property rights, we could be required to obtain a license from such third-party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors 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.

Third-party owned IP relating to CRISPR/Cas9 or other related technologies necessary to develop, manufacture and commercialize viable CRISPR/Cas9 therapeutics – such as compositions of the products or components, methods of treatment, delivery technologies, chemical modifications, and analytical and manufacturing methods – could adversely impact our ability to ultimately market and sell products. Third parties may own intellectual property, including patents, that cover all or aspects of our technologies and potential products, and may be necessary for us to develop or commercialize viable products. If we are unable to successfully license, avoid or challenge such third-party intellectual property, we may not be able to develop and commercialize viable products in all or certain jurisdictions. In addition, if the intellectual property covering our products or technologies that we own or license were to be legally impaired or lost, we may be unable to realize sufficient financial returns to support the development or commercialization of our products.

Under our license agreement with 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 recent proceedings, as well as potential future proceedings, related to this patent family may affect our ability to utilize the intellectual property sublicensed under our license agreement with Caribou.

The Broad Institute patent family includes issued patents in the U.S. and Europe that purport to cover certain aspects of the CRISPR/Cas9 genome editing platform for use on eukaryotic cells, including human cells. On June 25, 2019, the PTAB declared an interference between the UC/Vienna/Charpentier eukaryotic patent family and the Broad patent family that claim the use of the CRISPR/Cas9 technology in eukaryotic cells, including human cells. 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 inventorship evidence so that the PTAB can determine which research group first invented the use of the technology in eukaryotic cells and, therefore, is entitled to the patents covering the invention. As of September 30, 2020, 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. If the PTAB were to conclude that UC/Vienna/Charpentier were not the first inventors, we may not have rights to this invention, which could adversely impact our ability to develop and commercialize our product candidates. If it were to succeed in the interference, the Broad could seek to assert its issued patents against us based on our CRISPR/Cas9-based activities, including commercialization. Defense of these 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.

In addition, other third parties, such as Vilnius University, ToolGen, Inc., MilliporeSigma (a subsidiary of Merck KGaA) 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. In addition, UC/Vienna/Charpentier or the other third parties could seek judicial review of their inventorship claims. If UC/Vienna/Charpentier fail in defending their inventorship priority on any of these claims, 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. Even if we are successful in defending against such claims, any disputes could result in substantial costs and be a distraction to management and other employees.

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.

For example, as discussed above, on September 26, 2019, we announced that an arbitration panel had issued an interim award concluding that both the structural and chemical guide RNAs modification technologies were exclusively licensed to us by Caribou pursuant to the Caribou License. After concluding that the chemical modification technology was within the scope of our exclusive license with Caribou, the arbitration panel noted that its decision could delay or otherwise adversely impact the development of these modified guide RNAs as human therapeutics. Thus, solely with respect to the particular modified guide RNAs, the arbitration panel stated that it will declare that Caribou has an equitable award, which it described as exclusive, perpetual and worldwide. Upon, and subject to the terms of, a final award, which will follow further legal proceedings between the parties, Caribou could be able to use the modified guide RNAs at issue for certain human therapeutics. Although the interim award has no effect on our rights or current programs nor on Caribou's obligations under the Caribou License, we cannot predict the potential implications and impact the interim award may have on our business.

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 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. For example, a number of third parties have filed oppositions challenging the validity, and seeking the revocation, of the CRISPR/Cas9 genome editing patents granted to UC/Vienna/Charpentier by the European Patent Office to date. For example, third parties may continue to seek to challenge on appeal the validity of UC/Vienna/Charpentier’s 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, even though the European Patent Office (“EPO”) reaffirmed the validity of substantially all the claims after hearing the challenges of these third parties in January 2020. If UC/Vienna/Charpentier fail in defending the validity of this patent on appeal (or, at hearings before the European Patent Office’s Opposition Division on their other European patents that have similarly been opposed), 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. 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. For example, as discussed above, on September 26, 2019, we announced that an arbitration panel had issued an interim award concluding that both the structural and chemical guide RNAs modification technologies were exclusively licensed to us by Caribou pursuant to the Caribou License. Nevertheless, the arbitration panel noted that its decision could delay or otherwise adversely impact the development of these modified guide RNAs as human therapeutics. Thus, solely with respect to the particular modified guide RNAs, the arbitration panel stated that it will declare that Caribou has an equitable award, which it described as exclusive, perpetual and worldwide. Upon, and subject to the terms of, a final award, which will follow further legal proceedings between the parties, Caribou could be able to use the modified guide RNAs at issue to develop engineered CAR-T cells directed at CD19 as human therapeutics. Although the interim award has no effect on our rights or current programs nor on Caribou's obligations under the Caribou License, we cannot predict the potential implications and impact the interim award may have.

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, various third parties have filed challenges to the validity of UC/Vienna/Charpentier's European patents, which cover compositions comprising Cas9 and gRNA molecules, as well as methods of editing DNA *in vitro* or *ex vivo* using Cas9 and gRNAs. If UC/Vienna/Charpentier fail in defending the validity of these patents, we may lose valuable intellectual property rights, such as the exclusive right to use such intellectual property. Such an outcome could have a material adverse effect on our business in Europe.

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

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

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

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or future, potential customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to

ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Risks Related to Confidentiality

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

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect our proprietary and confidential information. We also utilize proprietary processes for which it would be difficult to enforce patents. In addition, other elements of our product discovery and development processes involve proprietary know-how, information, or technology that is not covered by patents. Trade secrets, however, may be difficult to protect. We seek to protect our proprietary processes, in part, by entering into confidentiality agreements with our employees, consultants, outside scientific advisors, contractors, and collaborators, and we also rely on 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.

In May 2016, we closed our initial public offering. Prior to this offering, there was no public market for our common stock. Although we have completed our initial public offering and shares of our common stock are listed and trading on the Nasdaq Global Market, an active trading market for our shares 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 patent applications, issued patents 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, acquire or in-license 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, companies trading in the stock market in general, and in the Nasdaq Global Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. 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, 2020, our executive officers, directors, 5% or greater stockholders and their affiliates beneficially owned approximately 62% 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 and cash equivalents and may not use them effectively.

Our management has broad discretion to use our cash and cash equivalents 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 and cash equivalents 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.

We could be subject to significant legal proceedings which may adversely affect our results of operations or financial condition.

We are subject to the risk of litigation, derivative claims, securities class actions, regulatory and governmental investigations and other proceedings, including proceedings arising from investor dissatisfaction with us or our performance. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. In addition, if any individuals acting on our behalf fails to satisfy his or her relevant legal or contractual duties, we could have liability to third-parties, including the government or investors. If any claims were brought against us and resulted in a finding of substantial legal liability, the finding could materially adversely affect our business, financial condition or results of operations or cause significant reputational harm to us, which could seriously adversely impact our business. Allegations of improper conduct by private litigants or regulators, regardless of veracity, also may harm our reputation and adversely impact our ability to grow our business. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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 and June 2020. 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 October 12, 2018, we filed a Shelf Registration Statement on Form S-3 (the "2018 Shelf") with the SEC in relation to the registration of common stock, preferred stock, warrants and units of any combination thereof for the purposes of selling, from time to time, our common stock, convertible securities or other equity securities in one or more offerings. We also simultaneously entered into an Open Market Sale Agreement (the "2018 Sales Agreement") with Jefferies LLC (the "Sales Agent"), to provide for the offering, issuance and sale of up to an aggregate amount of \$100.0 million of our common stock from time to time in "at-the-market" offerings under the 2018 Shelf and subject to the limitations thereof. We have paid the Sales Agent cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2018 Sales Agreement. In November 2018, we issued 1,659,300 shares of our common stock at \$18.00 per share in accordance with the 2018 Sales Agreement for net proceeds of \$28.5 million, after payment of cash commissions to the Sales Agent and approximately \$0.4 million related to legal, accounting and other fees in connection with the sales. During the twelve months ended December 31, 2019, we issued an additional 4,231,348 shares of our common stock, in a series of sales, at an average price of \$16.57 per share, in accordance with the 2018 Sales Agreement, for aggregate net proceeds of \$67.8 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. All shares related to the 2018 Sales Agreement had been sold as of December 31, 2019.

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 nine months ended September 30, 2020, we issued 1,107,100 shares of our 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 the Sales Agent 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. 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 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, 2019, we had federal and state NOLs of \$229.9 million and \$236.8 million, respectively, which begin to expire in 2034. As of December 31, 2019, we had federal and state research and development and other credit carryforwards of approximately \$12.6 million and \$8.7 million, which begin to expire in 2035 and 2031, 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. NOLs generated in taxable years ending after December 31, 2017 are not subject to expiration.

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	<u>Certification of 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.</u> (1)
31.2	<u>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.</u> (1)
32.1	<u>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.</u> (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 5, 2020

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)

**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 5, 2020

/s/ John M. Leonard

John M. Leonard, M.D.

President and Chief Executive Officer
(Principal Executive Officer)

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

I, Glenn Goddard, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Intellia Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 5, 2020

/s/ Glenn Goddard

Glenn Goddard

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

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

In connection with this Quarterly Report on Form 10-Q of Intellia Therapeutics, Inc. (the “Company”) for the period ended September 30, 2020, 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 5, 2020

/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)