Intellia Therapeutics, Inc.
Form 10-Q
May 02, 2019

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 March 31, 2019

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)	36-4785571 (I.R.S. Employer Identification No.)
40 Erie Street, Suite 130, Cambridge, Massachusetts (Address of Principal Executive Offices)	02139 (Zip Code)

857-285-6200

(Registrant’s Telephone Number, Including Area Code)

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

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

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

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

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

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

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

The number of shares outstanding of the registrant’s common stock as of April 30, 2019: 45,710,925 shares.

PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

INTELLIA THERAPEUTICS, INC.

Condensed Consolidated Balance Sheets (unaudited)

(Amounts in thousands except share and per share data)

	March 31, 2019	December 31, 2018
ASSETS		
Current Assets:		
Cash and cash equivalents	$47,097	$ 58,856
Marketable securities	249,485	255,203
Accounts receivable	3,591	7,547
Prepaid expenses and other current assets	3,520	3,371
Total current assets	303,693	324,977
Property and equipment, net	16,669	17,061
Operating lease right-of-use assets	21,012	-
Other assets	2,989	5,277
Total Assets	$344,363	$ 347,315
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$3,687	$ 2,708
Accrued expenses	7,735	10,742
Current portion of lease liability	4,381	-
Current portion of deferred revenue	23,431	27,122
Total current liabilities	39,234	40,572
Deferred revenue, net of current portion	25,659	28,810
Long-term lease liability	15,132	-
Other long-term liabilities	-	13
Commitments and contingencies		
Stockholders' Equity:		
Common stock, $0.0001 par value; 120,000,000 shares authorized; 45,479,098 and 45,224,480 shares issued and outstanding at March 31, 2019 and December 31, 2018, respectively	5	5
Additional paid-in capital	487,559	478,968
Accumulated other comprehensive income (loss)	59	(28)
Accumulated deficit	(223,285)	(201,025)
Total stockholders' equity	264,338	277,920
Total Liabilities and Stockholders' Equity	$344,363	$ 347,315

See notes to condensed consolidated financial statements.

INTELLIA THERAPEUTICS, INC.

Condensed Consolidated Statements of Operations and Comprehensive Loss (unaudited)

(Amounts in thousands except per share data)

	Three Months Ended March 31,	
	2019	2018
Collaboration revenue	$10,433	$7,469
Operating expenses:		
Research and development	23,709	22,493
General and administrative	10,533	7,406
Total operating expenses	34,242	29,899
Operating loss	(23,809)	(22,430)
Interest income	1,869	1,074
Net loss	$(21,940)	$(21,356)
Net loss per share, basic and diluted	$(0.49)	$(0.51)
Weighted average shares outstanding, basic and diluted	45,234	42,043
Other comprehensive loss:		
Unrealized gain on marketable securities	87	-
Comprehensive loss	$(21,853)	$(21,356)

See notes to condensed consolidated financial statements.

INTELLIA THERAPEUTICS, INC.

Condensed Consolidated Statements of Cash Flows (unaudited)

(Amounts in thousands)

	Three Months Ended March 31,	
	2019	2018
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$(21,940)	$(21,356)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,299	1,012
Loss on disposal of property and equipment	1	-
Equity-based compensation	4,592	4,107
Accretion of investment discounts	(1,422)	-
Non-cash lease expense	218	-
Changes in operating assets and liabilities:		
Accounts receivable	3,956	3,005
Prepaid expenses and other current assets	(150)	1,205
Accounts payable	1,356	59
Accrued expenses	(2,605)	(1,609)
Deferred revenue	(6,842)	(4,474)
Other assets	84	318
Other long-term liabilities	-	(37)
Net cash used in operating activities	(21,453)	(17,770)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	(1,533)	(1,850)
Purchases of marketable securities	(19,272)	-
Maturities of marketable securities	26,500	-
Net cash provided by (used in) investing activities	5,695	(1,850)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from common stock offering, net of offering costs	3,639	-
Proceeds from options exercised	360	6,720
Net cash provided by financing activities	3,999	6,720
Net decrease in cash and cash equivalents	(11,759)	(12,900)
Cash and cash equivalents, beginning of period	58,856	340,678
Cash and cash equivalents, end of period	$47,097	$327,778
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Purchases of property and equipment unpaid at period end	$446	$703

See notes to condensed consolidated financial statements.

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INTELLIA THERAPEUTICS, INC.

Notes to Condensed Consolidated Financial Statements (unaudited)

1. Overview and Basis of Presentation

Intellia Therapeutics, Inc. ("Intellia" or the "Company") is a genome editing company focused on developing 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"). The Company believes that CRISPR/Cas9 technology has the potential to transform medicine by editing disease-associated genes with a single treatment course, and that it can also be used to create novel engineered cell therapies that can replace a patient's diseased cells or effectively target various cancers and autoimmune diseases. The Company is leveraging its leading scientific expertise, clinical development experience and intellectual property ("IP") position to unlock a broad set of therapeutic applications for CRISPR/Cas9 genome editing and to develop a potential new class 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, 2018.

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.

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 our inception through March 31, 2019, we have raised an aggregate of $572.3 million to fund our operations, of which $143.1 million was through our collaboration agreements, $170.5 million was from our initial public offering and concurrent private placements, $141.0 million was from a follow-on public offering, $85.0 million was from the sale of convertible preferred stock and $32.7 million was from an at-the-market offering.

On October 12, 2018, the Company filed a Registration Statement on Form S-3 (the "Shelf") with the SEC in relation to the registration of common stock, preferred stock, warrants and/or units of any combination thereof (collectively, the "Securities"). The Company also simultaneously entered into an Open Market Sale Agreement (the "Sales Agreement") with Jefferies LLC, (the "Sales Agent"), to provide for the offering, issuance and sale by the Company of up to an aggregate amount of $100.0 million of its common stock from time to time in "at-the-market" offerings under the Shelf and subject to the limitations thereof. The Company will pay to the Sales Agent cash commissions of 3.0 percent of the gross proceeds of sales of common stock under the Sales Agreement. In November 2018, the Company issued

1,659,300 shares of its common stock at $18.00 per share in accordance with the Sales Agreement for net proceeds of $28.5 million, after payment of cash commissions of 3.0 percent of the gross proceeds to the Sales Agent and approximately $0.4 million related to legal, accounting and other fees in connection with the sale. In March 2019, the Company issued an additional 223,818 shares of its common stock, in a series of sales, at an average price of $17.32 per share, in accordance with the Sales Agreement, for aggregate net proceeds of $3.6 million, after payment of cash commissions of 3.0 percent of the gross proceeds to the Sales Agent and approximately $0.1 million related to legal, accounting and other fees in connection with the sales.

2. Summary of Significant Accounting Policies

The Company's significant accounting policies are described in Note 2, "Summary of Significant Accounting Policies", in our Annual Report. There have been no material changes during the three months ended March 31, 2019, other than the Company's adoption of Accounting Standards Codification ("ASC") 842 (as defined below) which is discussed in detail in this note.

Marketable Securities

The following table summarizes the Company's available-for-sale marketable securities as of March 31, 2019 and December 31, 2018 at net book value:

	March 31, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(In thousands)			
Short-term marketable securities:				
U.S. Treasury securities	$166,789	$ 33	$ -	$ 166,822
Financial institution debt securities	65,699	25	-	65,724
Corporate debt securities	16,938	1	-	16,939
Total	$249,426	$ 59	$ -	$ 249,485

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(In thousands)			
Short-term marketable securities:				
U.S. Treasury securities	$165,959	$ 2	$ (13)	$ 165,948
Financial institution debt securities	65,436	1	(17)	65,420
Corporate debt securities	23,836	-	(1)	23,835
Total	$255,231	$ 3	$ (31)	$ 255,203

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At March 31, 2019 and December 31, 2018, the balance in the Company's accumulated other comprehensive income (loss) was composed of activity related to the Company's available-for-sale marketable securities. There were no realized gains or losses in the period ended March 31, 2019, and as a result, the Company did not reclassify any amounts out of accumulated other comprehensive income (loss) during the period. The Company did not have any securities in an unrealized loss position at March 31, 2019.

Leases

Effective January 1, 2019, the Company adopted ASC Topic 842, Leases ("ASC 842"), using the required modified retrospective approach and utilizing the effective date as its date of initial application, for which prior periods are

presented in accordance with the previous guidance in ASC Topic 840, Leases.

At the inception of an arrangement, the Company determines whether an arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Most leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company has elected not to recognize on the balance sheet leases with terms of 12 months or less. The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to extend a lease are not included in the Company's assessment unless there is reasonable certainty that the Company will renew. The Company monitors its plans to renew its material leases on a quarterly basis.

Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in the Company's leases is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. In transition to ASC 842, the Company utilized the remaining lease term of its leases in determining the appropriate incremental borrowing rates.

In accordance with ASC 842, components of a lease should be allocated between lease components (e.g., land, building, etc.) and non-lease components (e.g., common area maintenance, consumables, etc.). The fixed and in-substance fixed contract consideration must be allocated based on the respective relative fair values to the lease components and non-lease components.

Although separation of lease and non-lease components is otherwise required, certain expedients are available. For new and amended leases beginning in 2019 and after, the Company has elected to account for the lease and non-lease components for leases for classes of all underlying assets and allocate all of the contract consideration to the lease component only.

Revenue Recognition

The Company adopted Accounting Standards Update ("ASU") No. 2014-09, Revenue from Contracts with Customers (Topic 606) and its related amendments (collectively known as "ASC 606") on January 1, 2018 using the modified retrospective method.

At inception, the Company determines whether contracts are within the scope of ASC 606 or other topics. For contracts that are determined to be within the scope of ASC 606, revenue is recognized when a customer obtains control of promised goods or services. The amount of revenue recognized reflects the consideration to which the Company expects to be entitled to receive in exchange for these goods and services. To achieve this core principle, the Company applies the following five steps (i) identify the contract with the customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when or as the Company satisfies a performance obligation. The Company only applies the five-step model to contracts when the Company determines that collection of substantially all consideration for goods and services that are transferred is probable based on the customer's intent and ability to pay the promised consideration.

Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct and are distinct in the context of the contract. To the extent a contract includes multiple promised goods and services, the Company applies judgment to determine whether promised goods and services are both capable of being distinct and distinct in the context of the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation.

The transaction price is determined based on the consideration to which the Company will be entitled in exchange for transferring goods and services to the customer. To the extent the transaction price includes variable consideration, the Company estimates the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method, depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in the Company's judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Any estimates, including the effect of the constraint on variable consideration, are evaluated at each reporting period for any changes. Determining the transaction price requires significant judgment, which is discussed in further detail for each of the Company's

collaboration agreements in Note 5. In addition, neither of the Company's contracts as of March 31, 2019 contained a significant financing component.

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation on a relative standalone selling price basis unless the transaction price is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation. The consideration to be received is allocated among the separate performance obligations based on relative standalone selling prices. The Company typically determines standalone selling prices using an adjusted market assessment approach model.

The Company satisfies performance obligations either over time or at a point in time. Revenue is recognized over time if either (i) the customer simultaneously receives and consumes the benefits provided by the entity's performance, (ii) the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or (iii) the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date. If the entity does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer.

As of March 31, 2019, the Company's only revenue recognized is related to collaboration agreements with third parties which are either within the scope of ASC 606, under which the Company licenses certain rights to its product candidates to third parties, or within the scope of ASC 808, Collaborative Arrangements ("ASC 808"), if it involves a joint operating activity pursuant to which the Company is an active participant and is exposed to significant risks and rewards with respect to the arrangement. For the collaboration arrangements under the scope of ASC 606, as discussed in further detail in Note 5, the terms of these arrangements typically include payment to the Company of one or more of the following: nonrefundable, upfront fees; development, regulatory, and commercial milestone payments; research and development funding payments; and royalties on the net sales of licensed products. Each of these payments results in collaboration revenues, except for revenues from royalties on the net sales of licensed products, which are classified as royalty revenues. For arrangements within the scope of ASC 808, the terms of these arrangements typically include payments received or made under the cost sharing provisions which are recognized as a component of revenues in the condensed consolidated statements of operations and comprehensive loss.

Licenses of intellectual property: If the license to the Company's IP is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from consideration allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the licenses. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone payments: At the inception of each arrangement that includes development milestone payments, the Company evaluates the probability of reaching the milestones and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur in the future, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received and therefore revenue recognized is constrained as management is unable to assert that a reversal of revenue would not be possible. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenues and earnings in the period of adjustment.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on levels of sales, if the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its collaboration agreements.

The Company receives payments from its customers based on billing schedules established in each contract. The Company's contract liabilities consist of deferred revenue. Upfront payments and fees are recorded as deferred revenue upon receipt or when due and may require deferral of revenue recognition to a future period until the Company satisfies its obligations under these arrangements.

The Company also considers the nature and contractual terms of an arrangement and assesses whether the arrangement involves a joint operating activity pursuant to which the Company is an active participant and is exposed to significant risks and rewards with respect to the arrangement. If the Company is an active participant and is exposed to the significant risks and rewards with respect to the arrangement, the Company accounts for the arrangement under ASC 808. Based on this consideration, the Company accounts for its Co-Development and Co-Promotion Agreement ("Co/Co") with Regeneron Pharmaceuticals, Inc. ("Regeneron") under ASC 808. Because ASC 808 does not provide recognition and measurement guidance for collaborative arrangements, the Company has analogized to ASC 606. Refer to Note 5 for additional information regarding the Company's collaboration agreements.

The following table presents changes in the Company's contract liabilities during the three months ended March 31, 2019 and 2018 (in thousands):

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Three Months Ended March 31, 2019				
Contract liabilities:				
Deferred revenue	$ 55,932	$ 1,000	$ (7,842)	$ 49,090

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Three Months Ended March 31, 2018				
Contract liabilities:				
Deferred revenue	$ 59,868	$ 1,000	$ (5,474)	$ 55,394

During the three months ended March 31, 2019 and 2018, the Company recognized the following revenues as a result of changes in the contract liability balance (in thousands):

Revenue recognized in the period from:	Three Months Ended March 31, 2019	Three Months Ended March 31, 2018
Amounts included in the contract liability at the beginning of the period	$ 7,842	$ 5,474

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.

Recent Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board ("FASB") issued ASU No. 2016-02, Leases ("ASU 2016-02"). ASU 2016-02 established ASC 842, which amends ASC Topic 840, Leases, by introducing a lessee model that requires balance sheet recognition for most leases and the disclosure of key information about leasing arrangements. Leases will be classified as finance or operating, with classification affecting the pattern and classification of expense recognition in the income statement. ASC 842 was subsequently amended during 2018. The Company adopted the new standard using the required modified retrospective approach on January 1, 2019 and used the effective date as its date of initial application. Consequently, financial information is not to be updated and the disclosures required under the new standard are not to be provided for dates and periods prior to January 1, 2019.

ASC 842 provides several optional practical expedients in transition. The Company elected the package of practical expedients which allows the Company to not reassess its existing conclusions on lease identification, classification, and initial direct costs. Further, the Company elected the hindsight practical expedient and utilized the short-term lease exemption for all leases with an original term of 12 months or less, for purposes of applying the recognition and measurement requirements of the new standard. The Company also elected the practical expedient which allows it to not separate lease and non-lease components for all its leases.

The adoption of the new standard resulted in the recognition of operating lease liabilities of $20.6 million, and right-of-use assets of $22.3 million on the Company's balance sheet relating to its leases. Further, an adjustment to retained earnings of $0.3 million was recognized due to the use of hindsight being applied in updating the lease term for one of the Company's property leases. The adoption of the standard did not have a material effect on the Company's condensed consolidated statements of operations and comprehensive loss or condensed consolidated statements of cash flows.

Refer to Note 6, “Leases”, for the Company’s current lease commitments.

In June 2018, the FASB issued ASU 2018-07, Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting, which simplifies the accounting for share-based payments to nonemployees by aligning it with the accounting for share-based payments to employees, with certain exceptions. The Company adopted the new standard beginning January 1, 2019; it did not have a material impact to the Company’s condensed consolidated financial statements.

In August 2018, the FASB issued 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 removes certain disclosures, modifies certain disclosures and adds additional disclosures related to fair value measurement. The new standard will be effective beginning January 1, 2020 and early adoption is permitted. The Company is currently evaluating the potential impact ASU 2018-13 may have on its disclosures upon adoption.

3. 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.

The Company’s financial instruments as of March 31, 2019 and December 31, 2018 included cash and cash equivalents, marketable securities, accounts receivable and accounts payable. As of March 31, 2019 and December 31, 2018, the Company’s financial assets recognized at fair value on a recurring basis consisted of the following:

	Fair Value as of March 31, 2019			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	$40,554	$40,554	$-	$ -
Marketable securities	249,485	166,822	82,663	-
Total	$290,039	$207,376	$82,663	$ -

	Fair Value as of December 31, 2018			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	$45,986	$45,986	$-	$ -
Marketable securities	255,203	165,948	89,255	-
Total	$301,189	$211,934	$89,255	$ -

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, we did not adjust or override any fair value measurements provided by the pricing services as of March 31, 2019 or December 31, 2018.

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

4. Accrued Expenses

Accrued expenses consisted of the following:

	March 31, 2019	December 31, 2018
	(In thousands)	
Employee compensation and benefits	$2,830	$ 6,175
Accrued research and development	2,231	2,328
Accrued legal and professional expenses	1,946	1,633
Accrued other	728	606
Total accrued expenses	$7,735	$ 10,742

5. 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.

Novartis Institutes for BioMedical Research

In December 2014, the Company entered into a strategic collaboration agreement with Novartis, as amended, (the "2014 Novartis Agreement") with Novartis primarily focused on the development of new ex vivo CRISPR/Cas9-edited therapies using chimeric antigen receptor T ("CAR-T") cells and hematopoietic stem cells ("HSC"s).

Agreement Structure. The parties agreed to engage in collaborative research activities using its CRISPR/Cas9 platform to identify and research therapeutic, prophylactic and palliative products and services relating to the following applications: a) ex vivo HSCs and b) ex vivo CAR-Ts. In addition, in the last two years of the collaboration term, Novartis may engage in research and development of a limited number of in vivo targets using the Company's platform.

Scope of Collaboration. During the five-year collaboration term parties may research potential therapeutic, prophylactic and palliative ex vivo applications of the CRISPR/Cas9 technology in HSCs and CAR-T cells. Research expenses incurred by the Company in support of the collaboration are reimbursed by Novartis.

HSC Program. The Company and Novartis agreed to conduct research of HSC targets under a research plan agreed upon by both parties. Within the HSC therapeutic space, Novartis may obtain exclusive rights to a limited number of these HSC targets, to be selected by Novartis in a series of selection windows. The Company has the right to choose a limited number of HSC targets for its exclusive development and commercialization per the specified selection schedule. Following these selections by Novartis and the Company, Novartis may obtain rights to research an additional limited number of HSC targets on a non-exclusive basis. Novartis is required to use commercially reasonable efforts to research, develop and commercialize at least one HSC product directed to each of their selected HSC targets.

CAR-T Program. The Company has also agreed to collaborate with Novartis on research activities for CAR-T cell targets. After completion of the activities contemplated by the parties' CAR-T cell program research plan, Novartis will assume sole responsibility for developing any products that it selects, arising from that research plan and the costs

and expenses of developing, manufacturing and commercializing its selected research targets. Novartis is required to use commercially reasonable efforts to research, develop or commercialize at least one CAR-T cell product directed to each of its selected CAR-T cell targets.

In Vivo Program. During the last two years of the five-year collaboration term, Novartis has the option to select a limited number of targets for research, development and commercialization of in vivo therapies using the Company's CRISPR/Cas9 platform, on a non-exclusive basis. Following Novartis' selection of each in vivo target, Novartis may offer the Company the right to participate in the research and development of such targets, in which case an in vivo program research plan for such target will be entered into between the Company and Novartis. Novartis is required to use commercially reasonable efforts to research, develop or commercialize at least one in vivo product directed to each of its selected targets. Novartis' in vivo target selections are subject to certain restrictions, including that the targets, or all targets within a limited number of organs: (i) have not already been reserved by the Company pursuant to its limited right to do so under the agreement; (ii) are not the subject of a collaboration or pending collaboration with a third party; and (iii) are not the subject of ongoing or planned research and development by the Company.

Governance. The parties formed HSC and CAR-T steering committees with responsibility for oversight of these respective research programs and approval of the associated research plans. Beginning in December 2018, the HSC steering committee became responsible for the ocular stem cell ("OSC") program. These steering committees in turn are overseen by a joint steering committee. The above steering committees are comprised by an equal number of representatives from each party.

Financial Terms. The Company received an upfront technology access payment from Novartis of $10.0 million in January 2015 and was entitled to additional technology access fees of $20.0 million and quarterly research payments of $1.0 million, or up to $20.0 million in the aggregate, during the five-year research term. To date, the Company has received $20.0 million in technology access fees and $16.0 million in research payments related to these programs. In addition, for each Novartis product under the collaboration (whether HSC or CAR-T, and beginning as of December 2018, OSC), subject to certain conditions, the Company may be eligible to receive (i) up to $30.3 million in development milestones, including for the filing of an investigational new drug ("IND") application and for the dosing of the first patient in each of Phase IIa, Phase IIb and Phase III clinical trials, (ii) up to $50.0 million in regulatory milestones for the product's first indication, including regulatory approvals in the U.S. and European Union ("EU"), (iii) up to $50.0 million in regulatory milestones for the product's second indication, if any, including U.S. and EU regulatory approvals, (iv) royalties on net sales in the mid-single digits, and (v) net sales milestone payments of up to $100.0 million. The Company is also eligible to receive payments for: (i) each additional HSC target selected by Novartis beyond its initial defined allocation, for which it will receive $1.0 million for each target, (ii) each in vivo target that Novartis selects as described above, and (iii) any exercise by Novartis of certain license options under the 2014 Novartis Agreement.

Upon completion of the research collaboration term in December 2019, Novartis has the option to internalize the Intellia platform for a $50.0 million fee, which will allow them to select a limited number of additional CRISPR/Cas9 genome editing targets over 5 years. Up to $20.0 million of the internalization fee will be credited towards any milestone payments for any additional post-internalization targets (up to $4.0 million per target).

Equity Investments. Additionally, at the inception of the arrangement, at which time the Company was a privately held company, Novartis invested $9.0 million to purchase the Company's Class A-1 and Class A-2 Preferred Units. The difference between the cash proceeds received from Novartis for the units and the $11.6 million estimated fair value of those units at the date of issuance was determined to be $2.6 million. Accordingly, $2.6 million of the upfront technology access payment was allocated to record the preferred units purchased by Novartis at fair value.

License Grant to Novartis. In the 2014 Novartis Agreement, the Company granted to Novartis a license to its CRISPR/Cas9 platform technology, including a sublicense to certain platform rights licensed from Caribou Biosciences, Inc. ("Caribou"), that is exclusive in the HSC, CAR-T cell and in vivo fields with respect to each target selected by Novartis pursuant to the agreement and the research plan as long as Novartis continues to use commercially reasonable efforts to research, develop, and commercialize CRISPR-edited products directed to such targets. Upon the expiration of the collaboration term, Novartis shall have the option to access and obtain a non-exclusive license to the Company's CRISPR/Cas9 platform technology to research, develop and commercialize potential therapeutic, prophylactic and palliative products and services for a limited number of certain approved targets selected by Novartis, exercisable upon written notice to the Company within 30 days after the expiration of the collaboration term. Such approved targets are subject to certain restrictions, including that the targets may not have been already reserved by the Company pursuant to its limited right to do so under the agreement, may not be the subject of an existing out license of the Company's CRISPR/Cas9 platform to a third party and may not be the subject of ongoing or planned research and development by the Company. This non-exclusive license will have a term of five years commencing upon the completion of the technology transfer by the Company enabling Novartis to practice such licensed rights, and Novartis may not select more than a specified number of approved targets in each year of this license term.

License Grant to Intellia. Novartis granted the Company a non-exclusive license to its IP covering small molecule for HSC expansion and to its LNP platform technology to research, develop and commercialize HSC and in vivo genome editing products, respectively, in the 2014 Novartis Agreement.

Intellectual Property. IP that the Company develops within the collaboration related to the Company's CRISPR/Cas9 platform will be owned solely by the Company, while all other IP developed within the collaboration, including IP covering products arising from the collaboration, will be jointly owned by the Company and Novartis.

2018 Amendment to the Agreement. In December 2018, the Company entered into an amendment to this agreement with Novartis (the "Amendment") which expands the scope of the 2014 Novartis Agreement to include the ex vivo development of CRISPR/Cas9-based cell therapies using limbal stem cells ("LSC"s), a type of OSC, primarily against gene targets selected by Novartis in exchange for a one-time payment of $10.0 million which the Company received in December 2018. The governance, milestones and royalties associated with any LSC program will follow those for the HSC programs. As part of the amendment, Intellia rights to Novartis' lipid nanoparticle ("LNP") technology were expanded to include use on all genome editing applications in both in vivo and ex vivo settings.

Term and Termination. The collaboration term ends in December 2019. The term of the agreement expires on the later of (i) the expiration of Novartis' payment obligations under the agreement and (ii) the date of expiration of the last-to-expire of the patent rights licensed to the Company or Novartis under the agreement. Novartis' 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 or (ii) 10 years after the first commercial sale of such product in such country. The Company may terminate the agreement if Novartis or its affiliates institute a patent challenge against its IP rights, and all improvements thereto, licensed to Novartis under the agreement. Novartis may terminate the agreement, without cause, upon 90 days' written notice to the Company subject to certain conditions, including its payment of any accrued and future obligations as if the collaboration had continued through December 2019. Either party may terminate the agreement in the event of the other party's uncured material breach or bankruptcy—or insolvency-related events.

Accounting Analysis. The Company has concluded that the 2014 Novartis Agreement and the Amendment are subject to ASC 606 and has assessed its accounting for them accordingly. The Company evaluated the promised goods and services under the 2014 Novartis Agreement and determined that it included two performance obligations: (1) a combined performance obligation representing a series of distinct goods and services including the licenses to research, develop and commercialize HSC products and their associated research activities and the licenses to research, develop and commercialize CAR-T cell products and their associated research activities; and (2) the preferred units.

The Company determined that the transaction price of the 2014 Novartis Agreement was $59.0 million consisting of the following consideration: (1) the upfront technology access payment of $10.0 million; (2) the additional technology access fees of $20.0 million; (3) the Company's estimate of variable consideration of $20.0 million related to the quarterly research payments; and (4) the payment for the preferred units of $9.0 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 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 Novartis and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price in each reporting period and when events whose outcomes are resolved or other changes in circumstances occur.

The Company first allocated $11.6 million of the transaction price to the preferred units to record the preferred units purchased by Novartis at fair value. The Company then allocated the remaining $47.4 million of the transaction price to the remaining combined performance obligation of the licenses and associated research activities for HSC and CAR-T cell products. Revenue allocated to the combined performance obligation of the licenses and associated research activities for HSC and CAR-T cell products is being recognized on a straight-line basis over a period of five years, which, in management's judgment, is the best measure of progress towards satisfying the performance obligation and represents the Company's best estimate of the period of the obligation.

The Company determined that there is only one combined performance obligation identified under the Amendment, representing a series of distinct goods and services including the licenses to research, develop and commercialize products using LSCs and their associated research and development services related to the research, development and commercialization of products using LSCs, and allocated the $10.0 million transaction price accordingly. Revenue allocated to this performance obligation is being recognized on a straight-line basis over a period of approximately one year, which, in management's judgment, is the best measure of progress towards satisfying the performance obligation and represents the Company's best estimate of the period of the obligation.

Revenue Recognition - Collaboration Revenue. Through March 31, 2019, 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 $54.4 million in cash and accounts receivable under the 2014 Novartis Agreement. Through March 31, 2019, the Company has recognized $43.6 million of collaboration revenue, including $4.7 million and $2.4 million during the three months ended March 31, 2019 and 2018, respectively, in the condensed consolidated statements of operations and comprehensive loss related to this agreement. As of March 31, 2019, there was approximately $13.8 million of the aggregate transaction price remaining to be recognized, which will be recognized through December 2019.

As of March 31, 2019 and December 31, 2018, the Company had accounts receivable of $1.0 million and $6.0 million, respectively, and deferred revenue of $10.8 million and $14.5 million, respectively, related to this agreement.

Regeneron Pharmaceuticals, Inc.

In April 2016, the Company entered into a license and collaboration agreement (the "Regeneron Agreement") with Regeneron.

Agreement Structure. The 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 and development 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.

Scope of Collaboration. Under the terms of the six-year collaboration, Regeneron may obtain exclusive rights for up to 10 targets to be chosen by Regeneron during the collaboration term, subject to a target selection process and various adjustments and limitations set forth in the agreement. Of these 10 total targets, Regeneron may select up to five non-liver targets, while the remaining targets must be focused in the liver. Certain non-liver targets from the Company's ongoing and planned research at the time, as well as any targets included in another of the Company's collaborations, are excluded from this collaboration. At the inception of the agreement, Regeneron selected the first of its 10 targets, transthyretin amyloidosis ("ATTR"), which is subject to a Co/Co between the Company and Regeneron, the general terms and conditions for which were outlined within the Regeneron Agreement.

Research Collaboration. Research activities under the collaboration 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 liver targets, and Regeneron will be responsible for preclinical research and conducting clinical development, manufacturing and commercialization of products directed to each of its exclusive 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 IND acceptance for at least one product directed to each applicable target, and following IND acceptance for at least one product, to develop and commercialize such product.

Reserved Liver Targets. The Company retains the exclusive right to solely develop products via CRISPR genome editing directed against certain specified genetic targets. 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 term may be subject to further co-development and co-commercialization arrangements at the Company or Regeneron's option, as applicable, which either can exercise pursuant to defined conditions.

Governance. The parties formed a joint steering committee, which is responsible for setting research objectives and overseeing the general strategies and activities undertaken by the parties under the Regeneron Agreement. Additionally, the parties formed a Joint Development and Commercialization Committee ("JDCC") to oversee all profit share products under the Co/Co discussed below. The JDCC will have responsibility for overseeing the development, manufacture, regulatory matters, and commercialization (including pricing and reimbursement) of ATTR, as the first profit share product under the collaboration agreement.

Financial Terms. The Company received a nonrefundable upfront payment of $75.0 million. In addition, on Regeneron programs that are not subject to co-development and co-promotion 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. In addition, Regeneron is obligated to fund 50.0 percent of the research and development costs for the ATTR program.

Equity Investments. In connection with this collaboration, 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 initial public offering.

Term and Termination. The collaboration term ends in April 2022, except that Regeneron may make a one-time payment of $25.0 million to extend the term for an additional two-year period. The agreement will continue until the date when no royalty or other payment obligations are due, unless earlier terminated in accordance with the terms of the agreement. 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) 12 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 agreement on a target-by-target basis if Regeneron does not proceed with the development of a product directed to a selected target within specified periods of time. Regeneron may terminate the agreement, 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 agreement. 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 12 years after the first commercial sale of any such products. Either party may terminate the agreement either in its entirety or with respect to the technology 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 Agreement. In July 2018, the Company and Regeneron finalized the form of the Co/Co that will be used as the basis for each Co/Co agreement directed to a target. Simultaneously, the Company and Regeneron executed the Co/Co agreement directed to the first collaboration target, ATTR, for which the Company will be the clinical and commercial Lead Party (see below). As such, Regeneron will be the Participating Party (see below) and will share equally in worldwide development costs and profits as long as it funds half of the defined research and development costs attributable to the ATTR program.

Co-Development and Co-Promotion: Agreement Structure. Under the Co/Co agreement, Regeneron has the right to exercise up to at least five Co/Co options on the Company's liver targets (other than the Company's reserved liver targets), while the Company may exercise at least one Co/Co option on Regeneron's liver targets, the exact number of Co/Co options being subject to certain conditions of the target selection process. Co/Co options must be exercised (or forfeited) once a target reaches a defined preclinical stage. Within 15 days of exercising the Co/Co option, the party exercising the option must pay $1.5 million to the other party as compensation for prior work. The ATTR program was exempted from this payment. One Party will be the "Lead Party" and the other Party the "Participating Party". The Lead Party shall have control and primary responsibility for the development, manufacturing, regulatory and commercial activities. The Participating Party shall have the right to consult on these activities through its participation on the JDCC and will have the right to co-fund development and commercialization activities in exchange for a share of profits. In general, 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 50.0 percent.

Co-Development and Co-Promotion: Termination. Either party may terminate by providing 180 days written notice. If the Company terminates, the product becomes a Regeneron product, and is subject to all future milestone and royalty payment obligations under the Regeneron agreement. If Regeneron terminates and has contributed at least $5.0 million in development costs, 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, if any, and Regeneron IP incorporated into the product.

Accounting Analysis. The Company determined that the Regeneron Agreement is within the scope of ASC 606. The Company evaluated the promised goods and services under the Regeneron Agreement and determined that the Regeneron Agreement included three performance obligations: (1) a combined performance obligation including the licenses to targets and the associated research activities and evaluation plans; (2) a combined performance obligation including the technology collaboration and associated research activities; and (3) the common stock.

The Company also concluded that the ATTR Co/Co meets the definition of a collaborative arrangement per 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 payments received or made under the cost sharing provisions of the ATTR Co/Co as a component of revenues in the condensed consolidated statements of operations and comprehensive loss.

Under the Regeneron Agreement, the Company determined that the transaction price was $125.0 million, consisting of the following consideration: (1) the nonrefundable upfront payment of $75.0 million; and (2) the payment for 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 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 will re-evaluate the transaction price in each reporting period and when events whose outcome are resolved or other changes in circumstances occur.

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 on a straight-line basis over the six-year performance period of the arrangement, which, in management's judgment, is the best measure of progress towards satisfying the performance obligation 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 on a straight-line basis 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 and represents the Company's best estimate of the period of the obligation.

Revenue Recognition – Collaboration Revenue. Through March 31, 2019, excluding the amounts allocated to Regeneron's purchase of common stock, the Company recorded a $75.0 million upfront payment and $14.7 million for research and development services under the Regeneron Agreement. Through March 31, 2019, the Company has recognized $51.3 million of collaboration revenue, including $5.7 million and $5.1 million during the three months ended March 31, 2019 and 2018, respectively, in the condensed consolidated statements of operations and comprehensive loss related to this arrangement. This includes $2.6 million and $2.0 million, respectively, representing payments due from Regeneron pursuant to the ATTR Co/Co, which is accounted for under ASC 808. As of March 31, 2019, there was approximately $38.3 million of the aggregate transaction price remaining to be recognized, which will be recognized ratably through April 2022.

As of March 31, 2019 and December 31, 2018, the Company had accounts receivable of $2.6 million and $1.5 million, respectively, and deferred revenue of $38.3 million and $41.4 million, respectively, related to this arrangement.

6.Leases

In October 2014, the Company entered into an agreement to lease office and laboratory space at 130 Brookline Street 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. Refer to Note 11, Subsequent Event, for additional information regarding this lease amendment. 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 applying the ASC 842 transition guidance, the Company retained the classification of this lease as operating and recorded a lease liability and a right-of-use asset on the ASC 842 effective date with the five-year extension included in the lease term, based on the Company's election of the hindsight practical expedient as the Company was reasonably certain to exercise this option term.

In March 2019, the Company entered into a separate agreement to sublease additional office and laboratory space at 130 Brookline Street in Cambridge, Massachusetts under an operating sublease agreement with a term through April 2021, with two options to extend the agreement by one-year each, for a total option period of up to two years. No right-of-use asset or lease liability has been recorded for this lease as of March 31, 2019, as the lease does not commence until April 2019. The Company estimates that at commencement it will recognize a right-of-use asset and lease liability between $1.0 million and $1.5 million.

In January 2016, the Company entered into a ten-year agreement to lease office and laboratory space at 40 Erie Street in Cambridge, Massachusetts under an operating lease agreement, with an option to terminate the lease at the end of the sixth year and an option to extend the term of the lease for an additional three years. Upon the execution of this lease, the Company provided a $2.2 million security deposit, which has been recorded in other assets on the condensed consolidated balance sheets. In addition, the Company had prepaid $2.2 million in lease payments as of December 31, 2018 under the terms of this lease. In applying the ASC 842 transition guidance, the Company retained the classification of this lease as operating and recorded a lease liability and a right-of-use asset on the ASC 842 effective date.

Throughout the term of its leases, the Company is responsible for paying certain costs and expenses, in addition to the rent, as specified in the lease, including a proportionate share of applicable taxes, operating expenses and utilities. The variable portion of these costs are expensed as incurred and are disclosed as variable lease cost.

The following table contains a summary of the lease costs recognized under Topic 842 and other information pertaining to the Company's operating leases for the three months ended March 31, 2019:

	(in thousands)	
Lease cost		
Operating lease cost	$ 1,703	
Variable lease cost	537	
Total lease cost	$ 2,240	
Other information		
Operating cash flows used for operating leases	$ 1,487	
Operating lease liabilities arising from obtaining right-of-use assets	-	
Weighted average remaining lease term	3.9 years	
Weighted average discount rate	9.00	%

Future minimum lease payments under the Company's non-cancelable operating leases as of March 31, 2019, are as follows:

Future Operating Lease Payments

Year Ending December 31,	(in thousands)
2019 (excluding the three months ended 3/31/19)	$ 4,980
2020	6,483
2021	6,618
2022	4,733
2023	871
Thereafter	943
Total lease payments	$ 24,628
Less: imputed interest	(3,655)
Less: leases not yet commenced	(1,460)
Total operating lease liabilities at March 31, 2019	$ 19,513

Future minimum lease payments under the Company's non-cancelable operating leases as of December 31, 2018, are as follows:

Year Ending December 31,	(In thousands)
2019	$ 5,616
2020	4,963
2021	5,507
2022	3,861
Thereafter	-
	$ 19,947

7.Equity-Based Compensation

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

	Three Months Ended March 31,	
	2019	2018
	(In thousands)	
Research and development	$1,783	$2,393
General and administrative	2,809	1,714
Total	$4,592	$4,107

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 three months ended March 31, 2019:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Unvested restricted stock as of December 31, 2018	109,073	$ 15.53
Granted	-	-
Vested	(29,881)	1.34

Cancelled	-		-
Unvested restricted stock as of March 31, 2019	79,192	$	20.89

As of March 31, 2019, there was $1.0 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 1.6 years.

Stock Options

The weighted average grant date fair value of options, estimated as of the grant date using the Black-Scholes option pricing model, was $8.94 per option and $18.28 per option for those options granted during the three months ended March 31, 2019 and 2018, respectively. Key assumptions used to apply this pricing model were as follows:

	Three Months Ended March 31,	
	2019	2018
Risk-free interest rate	2.6 %	2.5 %
Expected life of options	6.0 years	6.0 years
Expected volatility of underlying stock	69.2%	89.4 %
Expected dividend yield	0.0 %	0.0 %

The following is a summary of stock option activity for the three months ended March 31, 2019:

	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, 2018	5,037,663	$ 15.63		
Granted	446,333	14.13		
Exercised	(30,800)	11.64		
Forfeited	(121,742)	19.45		
Outstanding at March 31, 2019	5,331,454	$ 15.43	7.83	$ 18,628
Exercisable at March 31, 2019	2,073,239	$ 12.49	6.54	$ 11,814

As of March 31, 2019, there was $37.0 million of unrecognized compensation cost related to stock options that are expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 2.7

years.

Of the unvested restricted stock outstanding and stock options outstanding as of March 31, 2019, 71,875 are performance-based restricted stock units and 213,750 are performance-based stock options. The performance-based restricted stock units and performance-based stock options vest upon obtaining certain scientific and regulatory milestones through 2020. At March 31, 2019, 71,875 performance-based restricted stock units and 188,750 performance-based options are not included in computing the diluted (loss) earnings per share because the performance criteria had not been met as of the end of the reporting period.

8. Loss Per Share

The Company calculates basic (loss) earnings per share by dividing (loss) income by the weighted average number of common shares outstanding. The Company computes diluted (loss) earnings 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 March 31,	
	2019	2018
	(In thousands, except share data)	
Net loss	$(21,940)	$(21,356)
Weighted average shares outstanding, basic and diluted	45,234,326	42,042,586
Net loss per share, basic and diluted	$(0.49)	$(0.51)

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

	Three Months Ended March 31,	
	2019	2018
	(In thousands)	
Unvested restricted stock	79	400
Stock options	5,331	4,771
	5,410	5,171

9. Stockholders' Equity

The following tables present changes in stockholders' equity for the three-month periods ended March 31, 2019 and 2018 (in thousands, except share data):

			Accumulated	
		Additional	Other	Total

	Common Shares	Amount	Paid-In Capital	Comprehensive Income (Loss)	Accumulated Deficit	Stockholders' Equity (Deficit)
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 offering, 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 gain	-	-	-	87	-	87
Net loss	-	-	-	-	(21,940)	(21,940)
Balance at March 31, 2019	45,479,098	$ 5	$ 487,559	$ 59	$ (223,285)	$ 264,338

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	Common Shares	Amount	Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
Balance at December 31, 2017	42,384,623	$ 4	$ 421,706	$ -	$ (121,113)	$ 300,597
Retroactive adjustment to beginning accumulated deficit for adoption of ASU 2014-09	-	-	-	-	5,431	5,431
Exercise of stock options	709,321	-	6,720	-	-	6,720
Cancellation of restricted stock	(2,022)	-	-	-	-	-
Equity-based compensation	-	-	4,107	-	-	4,107
Net loss	-	-	-	-	(21,356)	(21,356)
Balance at March 31, 2018	43,091,922	$ 4	$ 432,533	$ -	$ (137,038)	$ 295,499

10. Related Party Transactions

Caribou Biosciences

In July 2014, the Company licensed from Caribou certain IP and entered into an arrangement under which Caribou provided research and development services. In addition, under the license agreement the Company agreed to pay 30 percent of Caribou's patent prosecution, filing and maintenance costs under its IP license agreement with Caribou. Caribou owned 5.5 percent of the Company's voting interests as of December 31, 2018 and 4.0 percent as of March 31, 2019.

On October 17, 2018, the Company initiated an arbitration proceeding with JAMS against Caribou asserting that Caribou is violating the terms and conditions of the license agreement, 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 the Company's exclusive human therapeutic field. Caribou has asserted that the two families of IP are outside the scope of the license agreement. In accordance with the Caribou License, the Company has submitted a demand for arbitration seeking a declaration that the disputed IP is included within the scope of the Company's license under the Caribou License, an award of compensatory, consequential and punitive damages based on Caribou's conduct, and an injunction prohibiting Caribou from licensing or using this IP in the Company's exclusive human therapeutics field, among other claims. The arbitration will take place in San Francisco, California with a decision expected during the third quarter of 2019.

The Company recognized general and administrative expense of $0.2 million during each of the three-month periods ended March 31, 2019 and 2018, respectively, related to the Company's obligation to pay 30 percent of Caribou's patent prosecution, filing and maintenance costs.

Novartis Institutes for BioMedical Research

In connection with its entry into the collaboration and license agreement and related equity transactions with Novartis, in 2015 the Company issued Novartis capital stock, and in May 2016, Novartis acquired 277,777 shares of the Company's common stock in a private placement transaction concurrent with the Company's IPO. As a result of these capital stock transactions, Novartis collectively owned 9.6 percent of the Company's voting interests as of March 31, 2019.

The Company recognized collaboration revenue of $4.7 million and $2.4 million during the three months ended March 31, 2019 and 2018, respectively, related to this agreement. As of March 31, 2019 and December 31, 2018, the Company had recorded accounts receivable of $1.0 million and $6.0 million, respectively, and deferred revenue of $10.8 million and $14.5 million, respectively, related to this collaboration. Refer to Note 5, Collaborations, for additional information regarding this collaboration agreement.

11. Subsequent Event

On April 5, 2019, the Company entered into a First Amendment to Lease (the "Lease Amendment") with MIT 130 Brookline Leasehold LLC (the "Landlord"). The Lease Amendment amends the Company's existing lease with the Landlord, dated as of October 21, 2014, as affected by a certain letter agreement dated June 12, 2015 (collectively, the "130 Brookline Lease"), pursuant to which the Company leased approximately 15,169 rentable square feet of space in the building located at 130 Brookline Street, Cambridge, Massachusetts.

Pursuant to the Lease Amendment, the Company exercised its option to extend the term of the 130 Brookline Lease by five years from the original expiration date of January 31, 2020 to January 31, 2025, unless earlier terminated in accordance with the terms of the 130 Brookline Lease (the "Extension Term"). Base rent will be approximately $0.1 million per month for the first 12 months following the commencement of the Lease Amendment, with three percent annual increases thereafter through the Extension Term. As an inducement to the Company entering into this Lease Amendment, the Landlord is providing a special tenant improvement allowance equal to approximately $0.2 million to be used by the Company solely for costs incurred by the Company for alterations to the premises performed in accordance with certain articles of the 130 Brookline Lease.

There were no other material changes to our contractual obligations and commitments, outside the ordinary course of business from those disclosed in our annual report, during the three months ended March 31, 2019. See Note 6, "Leases", for further information regarding our operating leases.

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 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:

- the initiation, timing, progress and results of our research and development programs and future preclinical and clinical studies, including the anticipated timing of an investigational new drug application for transthyretin amyloidosis, our lead in vivo indication;
- 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 timing or likelihood of regulatory filings and approvals;
- the commercialization of our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, and strategic plans for our business, product candidates and technology;
- 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;
- our financial performance or ability to obtain additional funding;
- developments relating to our licensors, licensees, third-parties from which we derive rights, collaborators, competitors and our industry; and

- other risks and uncertainties, including those listed under the caption "Risk Factors."

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

Management Overview

Intellia Therapeutics, Inc. ("we," "us," "our," "Intellia," or the "Company") is a leading genome editing company focused on developing 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 editing disease-associated genes with a single treatment course, and that it can also be used to create novel engineered cell therapies that can replace a patient's diseased cells or effectively target various cancers and autoimmune diseases. We leverage our leading scientific expertise, clinical development experience and intellectual property ("IP") position to unlock a broad set of therapeutic applications for CRISPR/Cas9 genome editing and to develop a potential new class 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 the Company's Annual Report on Form 10-K for the year ended December 31, 2018.

We aim to build a long-term company to fulfill our mission 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 the following 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 March 31, 2019, we have raised an aggregate of

approximately $572.3 million to fund our operations, of which $143.1 million was through our collaboration agreements, $170.5 million was from our initial public offering and concurrent private placements, $141.0 million was from a follow-on offering, $85.0 million was from the sale of convertible preferred stock and $32.7 million was from an at-the-market offering.

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 an early pipeline that reflects our full-spectrum approach and leverages the modularity inherent in our platform.

Our pipeline includes in vivo proprietary programs targeting genetic diseases, including transthyretin amyloidosis ("ATTR"), which we are co-developing with Regeneron Pharmaceuticals, Inc. ("Regeneron"), alpha-1 antitrypsin deficiency ("AATD"), and other disorders such as primary hyperoxaluria. Our pipeline also includes ex vivo programs consisting of two separate efforts: 1) a set of proprietary programs focused on engineered cell therapies to treat various cancers and autoimmune diseases, and 2) partnered programs developed in collaboration with Novartis Institutes for BioMedical Research, Inc. ("Novartis" or "NIBR"), focused on chimeric antigen receptor T cells ("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 in vivo programs focus on treating diseases attributable to genes expressed in the liver that have significant unmet medical needs – ATTR (which we are co-developing with Regeneron), AATD, and primary hyperoxaluria type 1 ("PH1"). 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 and guide RNA 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 ("TCR"s). Our goal for the ex vivo pipeline is to move from autologous to allogeneic therapies, and from blood to solid tumors. Our other ex vivo programs, which are partnered with Novartis, use CRISPR/Cas9 to research potentially allogeneic CAR-T cell therapies, as well as engineered HSC and OSC product candidates.

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.

The following table summarizes the status of our most advanced programs:

In Vivo Programs

Our initial in vivo indications target genetic liver diseases, including ATTR, AATD and PH1. 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 protein ("TTR") 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 symptoms, often including peripheral neuropathy and/or cardiomyopathy. Historically, hATTR with peripheral neuropathy was known as familial amyloidotic polyneuropathy, whereas hATTR with cardiomyopathy was known as familial amyloidotic cardiomyopathy. Typical onset of disease symptoms is during adulthood and can be fatal within two to 15 years. Estimates suggest that approximately 50,000 patients suffer from 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"), also known as senile systemic amyloidosis, 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.

Our lead candidate for the treatment of ATTR, NTLA-2001, which demonstrated an average of >95% reduction in circulating TTR protein in non-human primates ("NHP"s), has been nominated as our first in vivo development candidate to advance into Investigational New Drug ("IND")-enabling toxicology studies. Preliminary results from substantially completed dose-range finding studies showed a favorable tolerability profile; and data from multiple studies in NHPs demonstrated durable liver editing with sustained reduction of circulating TTR through 10 months of observation following a single dose. We recently announced plans to begin IND-enabling toxicology studies of NTLA-2001 in mid-2019 and that it remains on track to submit an IND application in 2020. NTLA-2001 is being co-developed with Regeneron; we are the lead development and commercialization party.

Alpha-1 Antitrypsin Deficiency – ("AATD")

AATD is an inherited genetic disorder that may cause lung and/or liver disease. The lung disease may result in chronic obstructive pulmonary disease ("COPD"), a progressive disorder that causes substantial morbidity and mortality. The liver disease, which is less common, is characterized by inflammation and cirrhosis of the liver. In the United States ("U.S."), an estimated 60,000 to 100,000 people have AATD, which is the result of a mutation in the SERPINA1 gene that normally produces alpha-1 antitrypsin ("A1AT") protein that is secreted into the blood. A1AT is a protease inhibitor that blocks the activity of various enzymes such as neutrophil elastase, which is an enzyme that fights infections, but when not adequately controlled by A1AT, can attack normal tissues, such as lung tissue.

The most common form of AATD arises when a patient has a mutation in both copies of the SERPINA1 gene, which causes A1AT to aggregate inside liver hepatocytes, rather than being secreted from the liver. The inability to secrete A1AT from the liver leaves the lung unprotected from neutrophil elastase and can result in pulmonary disease. The pulmonary consequences of AATD can sometimes culminate in COPD. Estimates suggest that between one and two percent of all cases of COPD in the U.S. have AATD as the underlying cause. In some instances of the disease, A1AT accumulates in the liver, causing liver inflammation and cirrhosis, which leads to liver damage, scarring and in the most severe cases, liver failure or cancer. Liver disease associated with AATD is diagnosed from infancy to adulthood, whereas lung disease is most common in adult patients.

Primary Hyperoxaluria type 1 – (“PH1”)

The primary hyperoxalurias are a group of autosomal recessive disorders that are associated with the overproduction of oxalate, a highly insoluble end-product of metabolism that is excreted almost entirely by the kidneys. The overproduction of oxalate leads to the recurrent formation of kidney and bladder stones as well as progressive renal damage (caused by a combination of nephrotoxicity induced by oxalate, obstructions caused by kidney stones and often superimposed infection). This progressive renal damage typically results in chronic kidney disease and ultimately end stage renal disease (“ESRD”).

PH1, one of three types of primary hyperoxaluria, is caused by a deficiency of the liver-specific peroxisomal enzyme alanineglyoxylate aminotransferase (“AGT”), which results in the accumulation of glyoxylate and excessive production of both oxalate and glycolate. PH1 is the most common form of primary hyperoxaluria, accounting for approximately 80 percent of cases, and it has an estimated prevalence of 1-3 cases per million population. PH1 can occur at almost any age, but typically presents during childhood. While kidney stone formation is often the first sign of disease, 20 to 50 percent of patients have advanced chronic kidney disease or even ESRD at the time of diagnosis. Data from the Rare Kidney Stone Consortium indicate that the median age at diagnosis of ESRD is 24 years, highlighting the progressive nature of the disease.

At the 2019 American Society of Gene and Cell Therapy (“ASGCT”) Annual Meeting, we presented new data demonstrating that independent CRISPR-mediated knockout of each of two targets of interest, either lactate dehydrogenase A (Ldha) or hydroxyacid oxidase 1 (Hao1), via our proprietary LNP delivery technology, results in a durable, therapeutically relevant reduction of oxalate excretion in a mouse model of PH1. We observed that CRISPR-mediated knockout of the Ldha gene in a PH1 mouse model disrupts LDHA protein production and reduces urinary oxalate levels by 63%. In a second distinct approach, we also observed that a CRISPR-mediated knockout of the Hao1 gene disrupts glycolate-to-glyoxylate conversion, resulting in a urinary oxalate level reduction of 57% in a PH1 mouse model. In each individual knockout approach of either Ldha or Hao1, these reduced levels of urinary oxalate were sustained for at least 15 weeks.

Gene Insertion

While knockout edits can be made using solely a Cas9 protein and guide RNA, other kinds of editing, involving repair and insertion, additionally require a template DNA that contains a desired sequence that may be inserted or used to correct the original sequence. For ex vivo applications, the DNA template may be delivered by electroporation in combination with a Cas9-guide RNA complex, or by other means such as viral vectors. For in vivo applications, we have developed combination approaches for delivering the editing machinery by LNP, and the repair and insertion templates by adeno-associated viral (“AAV”) vectors.

At the 2018 European Society of Gene and Cell Therapy (“ESCGT”), in a collaboration between Intellia and Regeneron, researchers combined our LNP delivery system of CRISPR/Cas9 with an AAV containing a proprietary bi-directional insertion template. Using the combination LNP-AAV insertion delivery system in mice, we achieved blood levels of human Factor IX (“FIX”) protein, produced by an inserted Factor 9 (“F9”) gene, corresponding to levels higher than those required in a clinical setting, after a single dose. FIX is a blood-clotting protein that is missing or defective in hemophilia B patients. This hybrid LNP-AAV delivery approach was then applied to our wholly owned AATD program to achieve CRISPR-mediated insertion of donor template DNA encoding the SERPINA1 gene. The insertion resulted in blood protein levels in mice that correspond to AAT blood levels that prevent progressive loss of pulmonary capacity in humans. These data show that the hybrid LNP-AAV delivery system can achieve targeted, stable insertion of DNA by combining the advantages of transient Cas9 expression via LNP-based delivery with AAV as a template delivery approach. These data further highlight the potential to simultaneously address a broad set of genetic diseases which may require complex edits.

Building on the data presented at the 2018 ESGCT Meeting, we presented data at the 2019 ASGCT Annual Meeting demonstrating the first CRISPR-mediated, targeted transgene insertion in the liver of NHPs, using F9 as a model gene. NHP data showed that a single administration achieved ~3-4 μg/mL of circulating human FIX protein at day 14 and was sustained through 28 days (~3-5 μg/mL) of completed observation in an ongoing study. The levels of circulating human FIX protein demonstrated in NHPs correspond with the normal 3-5 μg/mL range of human FIX protein levels (source: Amiral et al, Clin. Chem., 1984). The NHP data shared also incorporates the improved CRISPR/Cas9 LNP identified from the ATTR program. In addition, we also shared updated results from an ongoing durability study, first reported in October 2018 at ESGCT, that the circulating supratherapeutic human FIX protein levels achieved in mice with our hybrid LNP-AAV delivery system have remained stable through 10 months of observation.

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 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.
- Outside our Novartis collaboration, 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 Ospedale San Raffaele, a leading European research-university hospital, we are identifying optimized TCRs recognizing a tumor target that could be used to treat certain cancers.
- We are also exploring methods to apply CRISPR/Cas9 editing to CD4 cells to induce a non-reverting regulatory T cell phenotype, to create therapies that address auto-immune diseases.

For our ex vivo programs requiring delivery to isolated cells such as HSCs or T cells, we initially plan to deliver the CRISPR/Cas9 complex by electroporation. We are also exploring alternative technologies that may provide advantages in delivery efficiency or cell viability.

Acute myeloid leukemia - (“AML”)

AML includes a heterogeneous 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 an overall 5-year survival of less than 30 percent. 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. Specifically, it is estimated that there will be approximately 20,000 new cases of AML in the U.S. in 2019 as well as more than 10,000 deaths. 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.

Along with our research collaborators at IRCCS Ospedale San Raffaele, we presented new in vitro data at the 2019 ASGCT Annual Meeting showing that CRISPR/Cas9 editing resulted in >98% knockout of endogenous TCRs , while achieving transfer of various Wilms’ Tumor 1 (“WT1”)-specific TCRs into >95% of isolated T cells. In addition, the engineered T cells were functional and capable of specifically killing a panel of leukemic blasts from patients that expressed the WT1 epitope. Based on these results, we have identified multiple lead TCRs restricted to the HLA-A*02:01 allele to move into functional testing in patient-derived xenograft models for an autologous TCR-based therapy targeting WT1 for the treatment of AML. The studies are expected to begin in mid-2019 and will inform the nomination of our first engineered cell therapy development candidate by the end of 2019.

CAR-T Cell, HSC and OSC Research Collaboration with Novartis

Under our collaboration agreement with Novartis, we received an upfront technology access payment from Novartis of $10.0 million, and we are entitled to receive up to an additional $40.0 million, in aggregate, in additional technology access fees and research payments during the five-year collaboration term, subject to certain credits and adjustments in favor of Novartis. In addition, we received a $10.0 million payment relating to the expansion of the collaboration to include OSCs. 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. For more information regarding our ongoing collaboration with Novartis, see the section below entitled “Collaborations—Novartis.”

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CAR-T cell Program

In 2017, the first CAR-T cell products, including Novartis' Kymriah, were approved by the U.S. Food and Drug Administration ("FDA") to treat certain oncological indications such as pediatric acute lymphoblastic leukemia and Non-Hodgkins Lymphoma. Additional therapies are being developed for blood cancers such as AML, multiple myeloma and chronic lymphocytic leukemia, as well as several other solid-tumor cancers. In CAR-T cell therapy, naturally-occurring immune cells, specifically T cells, are modified ex vivo by inserting a CAR into the T cells, thereby redirecting their response towards cancer cells.

CAR-T cell products can benefit from the application of CRISPR/Cas9 in multiple ways, including:

- CRISPR/Cas9 could be used to create a universal donor CAR-T cell by knocking out cell surface markers that cause a patient's immune system to recognize another person's cells as foreign. Allowing multiple patients to be treated using cells from a single donor could significantly streamline manufacturing and make CAR-T cell therapy more widely accessible.
- CRISPR/Cas9 could be used to modify the T cells to enhance their survival or activity against cancer cells.
- CRISPR/Cas9 could be used to introduce the CAR into a precise location in the genome with a specific integrated copy number, as opposed to the current method involving semi-random integration, thus potentially improving the safety profile of the resulting cells.
- CRISPR/Cas9 could be used to knock out one or more of the proteins believed to be responsible for certain serious side effects that can result in dangerously high fevers or severe loss of blood pressure.

We could potentially combine two or more of these approaches to further enhance CAR-T cell therapy.

HSC Program

HSCs are the stem cells from which all of the various types of blood cells originate. The HSCs present in transplanted bone marrow, mobilized peripheral blood or cord blood can repopulate a patient's blood system. There are multiple potential opportunities for treating patients using engineered HSCs, including treating three common classes of blood-related disorders, such as hemoglobin disorders, including sickle cell disease and beta thalassemia; primary immune deficiencies, such as X-linked severe combined immunodeficiency; and bone marrow failures, such as Fanconi anemia. There are limited treatment options available for these types of blood disorders, and available options typically require chronic blood transfusions or bone marrow transplants. These procedures are associated with significant risk, including mortality. We believe the CRISPR/Cas9 system can be used to potentially provide curative benefits by correcting the underlying genetic defect in blood cells of patients with these disorders. In additional applications, normal HSCs may be engineered ex vivo using CRISPR/Cas9 to express a therapeutic protein, which is then administered to patients in need of that protein.

Challenges of developing stem cell products can include the relatively low quantity of available cells for treatment and a limited ability to expand HSCs ex vivo. We expect to counter these challenges, if necessary, by employing a proprietary small molecule for HSC expansion to which Novartis has granted us rights. This small molecule could allow us to generate larger numbers of HSCs for re-implantation in patients after editing. We expect that the application of this technology will improve the performance of the blood cell graft and improve patient outcomes and recovery times as more therapeutic cells can be administered.

We are pursuing a number of potential gene targets and therapeutic indications in collaboration with Novartis. Under our collaboration with Novartis, we and Novartis each have the right to designate a fixed number of HSC therapeutic targets during multiple selection windows, with Novartis having the right of first target selections. Our selection criteria for development programs include, among others, disease severity, existing treatment options, delivery efficiency, the nature of the genetic edit required and the expected performance of cells modified by the procedure.

Collaborations

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

Novartis Institutes for BioMedical Research, Inc. (“Novartis”)

As described in Note 5, “Collaborations—Novartis Institutes for BioMedical Research, Inc.,” in December 2014, we entered into a strategic collaboration agreement with Novartis, primarily focused on the development of new ex vivo CRISPR/Cas9-edited therapies using CAR-T cells and HSCs.

In December 2018, we entered into an amendment to this agreement with Novartis which expands the scope of the 2014 Novartis Agreement to include the ex vivo development of CRISPR/Cas9-based cell therapies using limbal stem cells (“LSC”s), a type of OSC, primarily against gene targets selected by Novartis in exchange for a one-time payment of $10.0 million which we received in December 2018.

Through March 31, 2019, we had recorded a total of $54.4 million in cash and accounts receivable under the 2014 Novartis Agreement. Through March 31, 2019, we have recognized $43.6 million of collaboration revenue, including $4.7 million and $2.4 million in the three months ended March 31, 2019 and 2018, respectively, in the condensed consolidated statements of operations related to this agreement. As of March 31, 2019 and December 31, 2018, we had accounts receivable of $1.0 million and $6.0 million, respectively, and deferred revenue of $10.8 million and $14.5 million, respectively, related to this agreement.

Regeneron Pharmaceuticals, Inc.

As described in Note 5, “Collaborations—Regeneron Pharmaceuticals, Inc.,” in April 2016, we entered into a license and collaboration agreement with Regeneron. The agreement includes 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 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. Under this 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.

Through March 31, 2019, we recorded a $75.0 million upfront payment and $14.7 million for research and development services under the Regeneron Agreement. Through March 31, 2019, we have recognized $51.3 million of collaboration revenue, including $5.7 million and $5.1 million during the three months ended March 31, 2019 and 2018, respectively. This includes $2.6 million and $2.0 million, respectively, representing payments due from Regeneron pursuant to the ATTR Co/Co, which is accounted for under ASU No. 2018-18, Collaborative Arrangements (“ASC 808”). As of March 31, 2019 and December 31, 2018, we had accounts receivable of $2.6 million and $1.5 million, respectively, and deferred revenue of $38.3 million and $41.4 million, respectively, related to this agreement.

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, facility-related expenses, overhead expenses, reagents, lab supplies, consumables and contract research services.

General and Administrative

General and administrative expenses consist primarily of salaries 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 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 March 31, 2019 and 2018

The following table summarizes our results of operations for the three months ended March 31, 2019 and 2018:

	Three Months Ended March 31,		Period-to-Period Change
	2019	2018	
	(in thousands)		
Collaboration revenue	$10,433	$7,469	$ 2,964
Operating expenses:			
Research and development	23,709	22,493	1,216
General and administrative	10,533	7,406	3,127
Total operating expenses	34,242	29,899	4,343
Operating loss	(23,809)	(22,430)	(1,379)
Interest income	1,869	1,074	795
Net loss	$(21,940)	$(21,356)	$ (584)

Collaboration Revenue

Collaboration revenue increased approximately $3.0 million to $10.4 million during the three months ended March 31, 2019, as compared to $7.5 million during the three months ended March 31, 2018. The increase in collaboration revenue during the three months ended March 31, 2019 is primarily caused by a $2.4 million increase related to an amendment to the Novartis Agreement, for which we received a one-time payment of $10.0 million in December 2018. Additionally, collaboration revenue increased in the three months ended March 31, 2019 due to increased research and development services related to our ATTR program with Regeneron, increasing to $2.6 million during the three months ended March 31, 2019 as compared to $2.0 million during the three months ended March 31, 2018.

During the three months ended March 31, 2019 and 2018, collaboration revenue consisted of amounts recognized from deferred revenue related to an upfront payment received and amounts for research and development services under the Regeneron collaboration as well as amounts recognized from deferred revenue related to upfront technology access payments for licenses, technology access fees and research funding under the Novartis collaboration.

Research and Development

Research and development expenses increased $1.2 million to $23.7 million during the three months ended March 31, 2019, as compared to $22.5 million during the three months ended March 31, 2018. This increase is primarily related to increases in personnel-related costs of $0.9 million, driven by our growth in headcount; $0.5 million in information technology and software costs related to our research and development activities; and $0.3 million in depreciation on lab equipment. These increases were offset in part by a $0.6 million decrease in stock-based compensation due to some of our earlier grants being fully vested and a decrease in research and development expenses of $0.3 million due to the timing of material expenditures.

Through 2019, we expect research and development expenses to increase as we continue to grow our research and development team and advance our ATTR program towards clinical development.

General and Administrative

General and administrative expenses increased $3.1 million to $10.5 million during the three months ended March 31, 2019, compared to $7.4 million during the three months ended March 31, 2018. This increase was primarily related to an increase of $1.4 million in personnel-related costs, which includes a $1.1 million increase in equity-based compensation expense, as we grew in headcount; and an increase of $1.3 million in legal fees, which were principally related to IP matters.

Through 2019, we expect general and administrative expenses to increase as we continue to support the research and development team and advance our research plans.

Interest Income

Interest income increased by approximately $0.8 million to $1.9 million during the three months ended March 31, 2019 as compared to $1.1 million during the three months ended March 31, 2018. This increase was caused by a change to our investment policy in late 2018, allowing for investment in marketable securities, as well as a general increase in interest rates.

Liquidity and Capital Resources

Since our inception through March 31, 2019, we have raised an aggregate of $572.3 million to fund our operations, of which $143.1 million was through our collaboration agreements, $170.5 million was from our initial public offering and concurrent private placements, $141.0 million was from a follow-on public offering, $85.0 million was from the sale of convertible preferred stock and $32.7 million was from an at-the-market offering. As of March 31, 2019, we had $296.6 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 milestones and the timing of achieving these milestones is dependent upon the outcome of our research and development activities and is uncertain at this time. Our rights to payments under our collaboration agreements are our only committed external source of funds.

At-the-Market Offering

On October 12, 2018, we filed a Shelf Registration Statement with the SEC in relation to the registration of common stock, preferred stock, warrants and/or 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 a Sales Agreement with our 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 Shelf Registration Statement and subject to the limitations thereof. In November 2018, we issued 1,659,300 shares of our common stock at $18.00 per share in accordance with the Sales Agreement for net proceeds of $28.5 million, after payment of cash commissions of 3.0 percent of the gross proceeds to the Sales Agent and approximately $0.4 million related to legal, accounting and other fees in connection with the sale. In March 2019, we issued 223,818 shares of our

common stock in a series of sales, at an average price of $17.32 per share, in accordance with the Sales Agreement, for aggregate net proceeds of $3.6 million, after payment of cash commissions of 3.0 percent of the gross proceeds to the Sales Agent and approximately $0.1 million related to legal, accounting and other fees in connection with the sales.

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 other regulatory expenses, patent prosecution filing and maintenance costs for our licensed IP and general overhead costs. During 2019, we expect our expenses to increase compared to prior periods in connection with our ongoing activities, particularly as we continue our research activities and advance our ATTR program towards clinical development.

Because our research programs are still in preclinical development 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 are entitled to research payments under our collaboration with Novartis and receive cost reimbursements from Regeneron for the ATTR program. 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. 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 March 31, 2019, as well as research and cost reimbursement funding from Novartis and Regeneron, will enable us to fund our ongoing operating expenses and capital expenditures into the first half of 2021, excluding any potential milestone payments or extension fees that could be earned and distributed under the collaboration agreements with Novartis and Regeneron 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 three months ended March 31, 2019 and 2018:

	Three Months Ended March 31,	
	2019	2018
	(In thousands)	

Net cash used in operating activities	$(21,453)	$(17,770)
Net cash provided by (used in) investing activities	$5,695	$(1,850)
Net cash provided by financing activities	$3,999	$6,720

Net cash used in operating activities

Net cash used in operating activities of $21.5 million during the three months ended March 31, 2019 primarily reflects increased spend in our research and development and general and administrative activities, offset in part by the receipt of $7.5 million in payments from our collaboration partners, Novartis and Regeneron. Net cash used in operating activities of $17.8 million during the three months ended March 31, 2018 primarily reflects increased spend in our research and development and general and administrative activities, offset in part by the receipt of $6.0 million from Novartis.

Net cash provided by (used in) investing activities

During the three months ended March 31, 2019, our investing activities provided net cash of $5.7 million. This increase was related primarily to the maturity of $26.5 million in marketable securities, offset in part by the purchase of $19.3 million in marketable securities. Additionally, cash of $1.5 million and $1.9 million was used during the three months ended March 31, 2019 and 2018, respectively, to purchase property and equipment as we grow our operations and build out our office and laboratory facilities.

Net cash provided by financing activities

During the three months ended March 31, 2019 and 2018, our net cash provided by financing activities was $4.0 million and $6.7 million, respectively. Net cash provided by financing activities during the three months ended March 31, 2019 includes $3.6 million in proceeds from an at-the-market offering, net of $0.2 million in commissions and offering costs, and $0.4 million in cash received from the exercise of stock options. Net cash provided by financing activities during the three months ended March 31, 2018 is made up of $6.7 million in cash received from the exercise of stock options.

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 other significant changes to our critical accounting policies from those which were discussed in our Annual Report on Form 10-K for the year ended December 31, 2018.

Recent Accounting Pronouncements

Please read Note 2 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

We have entered into a First Amendment to Lease (the “Lease Amendment”) with MIT 130 Brookline Leasehold LLC (the “Landlord”). The Lease Amendment amends our existing lease with the Landlord, dated as of October 21, 2014, as affected by a certain letter agreement dated June 12, 2015 (collectively, the “130 Brookline Lease”), pursuant to which we leased approximately 15,169 rentable square feet of space in the building located at 130 Brookline Street, Cambridge, Massachusetts.

Pursuant to the Lease Amendment, we exercised our option to extend the term of the 130 Brookline Lease by five years from the original expiration date of January 31, 2020 to January 31, 2025, unless earlier terminated in accordance with the terms of the 130 Brookline Lease (the “Extension Term”). Base rent will be approximately $0.1 million per month for the first 12 months following the commencement of the Lease Amendment, with three percent annual increases thereafter through the Extension Term. As an inducement to us entering into this Lease Amendment, the Landlord is providing a special tenant improvement allowance equal to approximately $0.2 million to be used by us solely for costs incurred by us for alterations to the premises performed in accordance with certain articles of the Lease.

There were no other material changes to our contractual obligations during the three months ended March 31, 2019. 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 on Form 10-K for the year ended December 31, 2018.

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 March 31, 2019, we had cash equivalents and marketable securities of $290.0 million consisting of interest-bearing money market accounts, commercial paper, 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 in short-term 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 clinical trial costs. We do not believe that inflation had a material effect on our results of operations during the three months ended March 31, 2019.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

The Company has established disclosure controls and procedures designed to ensure that information required to be disclosed in the reports that the Company files or submits 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 March 31, 2019.

Changes in Internal Control over Financial Reporting

No change in the Company's internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended March 31, 2019 that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting.

PART II - OTHER INFORMATION

Item 1. Legal Proceedings

In the ordinary course of business, we are from time to time involved in lawsuits, claims, investigations, proceedings, and threats of litigation related to intellectual property ("IP"), commercial arrangements and other matters, including the matter described below. 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.

Caribou Intellectual Property Arbitration

On October 17, 2018, we initiated an arbitration proceeding with JAMS against Caribou Biosciences, Inc. ("Caribou") asserting that Caribou is violating the terms and conditions of the license agreement entered into by the Company and Caribou in July 2014 (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. Under the Caribou License, Caribou granted to Intellia a worldwide, exclusive license to all of Caribou's IP relating to CRISPR/Cas9 technology for all therapeutic, prophylactic and palliative uses and applications for any or all diseases and conditions in humans, with the sole exceptions of anti-microbial and/or anti-fungal applications. The license encompassed all CRISPR/Cas9 IP developed or controlled by Caribou as of July 16, 2014 and through an IP cutoff date (January 30, 2018) that was necessary or useful for us to develop, manufacture or commercialize products in our field, as well as any technology developed by Caribou under a service agreement entered into by the Company and Caribou in July 2014. Caribou has asserted that the two families of IP are outside the scope of our license. In accordance with the Caribou License, we have submitted a demand for arbitration seeking a declaration that the disputed IP is included within the scope of our license under the Caribou License, an award of compensatory, consequential and punitive damages based on Caribou's conduct, and an injunction prohibiting Caribou from licensing or using this IP in our exclusive human therapeutics field, among other claims. The arbitration will take place in San Francisco, California with a decision expected during the third quarter of 2019.

"Item 3. Legal Proceedings" of our Annual Report on Form 10-K for the fiscal year ended December 31, 2018 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 on Form 10-K for the year ended December 31, 2018 and in other documents that we file with the SEC, in evaluating the Company 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 described below are not intended to be exhaustive and are not the only risks facing the Company. 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.

Risks Related to the Discovery, Development, Manufacturing and Commercialization of Product Candidates

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. Similarly, 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.

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 for preclinical testing and clinical studies from the FDA and other 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. Any product candidates 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 our manufacturing capabilities, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. Before obtaining marketing approval from regulatory authorities for the sale of a product candidate, we must conduct extensive clinical trials to demonstrate the safety, purity and potency, as well as the efficacy, of the product candidates in humans. We cannot be certain 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 approval from the U.S. Food and Drug Administration (“FDA”) and other regulatory authorities that have very limited or no experience with the clinical development of CRISPR/Cas9 therapeutics, and which may require additional significant testing or data compared to more traditional therapies;
- seeking and obtaining regulatory approval from the FDA and other regulatory authorities in light of no formal guidance regarding potential regulatory pathways for CRISPR/Cas9-based in vivo therapeutics, including preclinical and clinical requirements for clearance of an Investigational New Drug (“IND”) and, as appropriate thereafter, a Biologics License Application (“BLA”), or corresponding applications outside the U.S.;
- 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;
- establishing process development and manufacturing capabilities that can produce sufficient clinical and, if approved, commercial quantities of product candidates in accordance with the 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 engineered cell therapy products have changed and may continue to change in the future. To date, only a limited number of products that involve the in vivo genetic modification of patient cells have been approved globally;

- improper modulation, including insertion, of a gene sequence into a patient's chromosome could lead to cancer, other aberrantly functioning cells or other diseases, including death;
- transient expression of the Cas9 protein within patients' cells 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.

Further, because our ex vivo product candidates involve editing human cells and then manufacturing and 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 therapies may require unique products to be created for each patient and such individualistic manufacturing may be both inefficient and cost-prohibitive.

To date, only a few human clinical trials utilizing either in vivo or ex vivo CRISPR/Cas9-based therapeutics have been authorized in the U.S. and EU member states. Further, only a limited number of human clinical trials for in vivo therapies or engineered cell therapies developed using other genome-editing technologies have been authorized by the FDA in the U.S. or by the relevant regulatory agencies in the EU member states. There is no certainty that the FDA or the European Medicines Agency ("EMA") will apply to CRISPR/Cas9 product candidates the same regulatory pathway and requirements it is applying to other in vivo therapies or ex vivo engineered cell therapeutics; and the FDA and other regulatory authorities have not yet provided written guidance regarding preclinical or clinical studies or regulatory approval pathways specific for either in vivo or ex vivo genome editing-based therapeutics. In addition, if any product candidates encounter safety or efficacy problems, developmental 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, significant uncertainty exists regarding the future scope and effect of the FDA's regulatory framework, 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. Any such changes to the FDA requirements could impact our ability to obtain approval for our products or sell them profitably. In addition, in the EU, the decision of the United Kingdom to withdraw, whether it happens or not, from the EU has required the EMA to relocate to the Netherlands, and recruit and retain new personnel to review and approve our submissions for regulatory approval in Europe. EMA's relocation could result in delays and other changes that may impact our ability to obtain timely approval for our products in the EU. Also, upon exiting the EU, the United Kingdom 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 United Kingdom.

In addition, during fiscal year 2017, non-commercial entities commenced human trials involving in vivo CRISPR/Cas9-based therapeutics in China. Neither these entities nor the Chinese regulatory agencies have shared publicly any information on the regulatory process for clinical trial approval including specific protocol requirements. Any specific requirement from the Chinese regulatory agencies may impact our ability to submit or obtain approval for our products in China. Further, if these human trials (or the human trials that have been authorized in the U.S., EU or other nations) are unsuccessful, or if they result in significant adverse events, including deaths, there could be a significant impact to the evaluation of our product candidates globally, as well as an increase in negative public opinion.

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, EMA 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, EMA 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, EMA 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.

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, earlier 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 the Company, 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, recent reports of the use of CRISPR/Cas9 in China to edit embryos in utero has 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.

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 delayed in obtaining marketing approval for our future product candidates, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to 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.

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 or preclinical stage, and their risk of failure is high. 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 BLA to the FDA, a Marketing Authorization Application to the EMA and similar filings 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 ("IRB"s) 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 ("CRO"s), 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;
- 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.

We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, the Data Safety Monitoring Board ("DSMB") for such trial or the FDA or other 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.

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. (“Caribou”), Casebia Therapeutics, LLC, CRISPR Therapeutics, Inc., Editas Medicine, Inc., ToolGen, Inc., and Tracr Hematology Limited;
- other genome editing companies including: bluebird bio, Inc., Cellectis 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: bluebird bio, Inc., Cellectis S.A., Celgene Corporation (which acquired Juno Therapeutics, Inc.), Gilead Sciences, Inc. (which acquired Kite Pharma, Inc.), Novartis A.G., Spark Therapeutics, Inc., and Voyager Therapeutics, Inc.

Our competitors will also include companies that are or will be developing other genome editing methods as well as small molecules, biologics, in vivo gene therapies, engineered cell therapies (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 the value of the Company and could impair our ability to raise capital, maintain our research and development efforts,

expand our business or continue our operations.

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 any 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. 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 the value of the Company 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 an initial product candidate for clinical development for our transthyretin amyloidosis (“ATTR”) program, 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 appropriate for clinical development 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 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 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 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 third-party payors and government authorities;
    - 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 third-party payors and government authorities;
- 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.

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 and marketing 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.

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. 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.

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, and commercial payors are critical to new product acceptance.

Government authorities and 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. 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 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 the U.S. and abroad 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 both the U.S. and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the EU (and in the United Kingdom if and when it exits the EU), 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.

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 FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA, the EMA 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, the EMA 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 manufacture at the necessary scale and in compliance with regulatory requirements to support our clinical trials or, if approved, commercial efforts. In addition, we may have to 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.

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 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 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, and/or business partners, or from cyber-attacks by malicious third parties. 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 of future clinical trial participants, could harm our reputation, require us to comply with federal and/or state breach notification laws and foreign law equivalents, and otherwise subject us to liability 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 described above. While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business.

Risks Related to Our Financial Position and need for Additional Capital

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 a preclinical-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 stage. We have not yet demonstrated our ability to successfully initiate 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, including the EMA, 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 $21.9 million for the quarter ended March 31, 2019. As of March 31, 2019, we had an accumulated deficit of $223.3 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.

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

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.

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.

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

Inadequate funding for the FDA and other government agencies could hinder their ability to hire and retain 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 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 accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. 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 agencies may also slow the time necessary for new drugs 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, it could significantly impact the ability of 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

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.

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 cells ("CAR-Ts") 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 LSCs primarily against selected gene targets by Novartis.

In April 2016, we entered into a collaboration agreement with Regeneron that 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/Cas9 technology to enhance our genome editing platform. Pursuant to the Regeneron collaboration agreement, we granted Regeneron exclusive rights to select up to 10 targets, subject to certain restrictions, while we retain the rights to solely develop our initial indications, other than ATTR, which is subject to a co-development and co-promotion agreement with Regeneron. We also have the right to choose additional liver targets for our own development during the collaboration term. In July 2018, we entered into the first co-development and co-promotion agreement directed to ATTR, under which we will be the clinical and commercial lead for ATTR activities.

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 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.

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 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.

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 eventually rely on outside vendors, such as CMOs, to manufacture supplies and process our product candidates. We have not yet caused any product candidates to be manufactured or processed on a clinical or commercial scale, and may not be able to do so for any of 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 contract manufacturers to manufacture our product candidates must be inspected and approved by the FDA or other foreign regulatory agencies pursuant to inspections that will be conducted after we submit an application to the FDA or other foreign regulatory agencies. We will be dependent on our contract manufacturing 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 contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of 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 contract manufacturers 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 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.

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 and trial sites, 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 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 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.

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. 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.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms. Switching or adding additional CROs 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 our CROs, 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 Growth

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, José E. Rivera, our Executive Vice President, General Counsel, and Andrew Schiermeier, our Executive Vice President, Development and Corporate Strategy, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment arrangements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be important for our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products using our technology. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies, universities and research institutions for similar personnel. The market for qualified personnel in the biotechnology space generally, and genome editing and gene therapy fields in particular, in and around the Cambridge, Massachusetts area is especially competitive. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Further, some of the qualified personnel that we hire and recruit are not U.S. citizens, and there is uncertainty with regard to their future employment status due to the current U.S. administration's announced intention of modifying the legal framework for non-U.S. citizens to be employed in the U.S. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Risks Related to Government Regulation

While the regulatory framework for approval of gene therapy including genome editing products exists, the lack of 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 biologics, are subject to extensive regulation by the FDA in the U.S. and other regulatory authorities. We are not permitted to market any drug or biological product, including in vivo products or engineered cell therapies, in the U.S. until we receive regulatory approval from the FDA. We have not previously submitted a BLA to the FDA, or similar approval filings to comparable foreign authorities. A BLA 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 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, 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, and approval may not be obtained.

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;
- 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. Further, a clinical trial may be suspended or terminated by us, the IRBs for the institutions in which such trials are being conducted, 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.

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.

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, potency, efficacy 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, including ensuring that quality control and manufacturing procedures conform to cGMP and, in certain cases, cGTP requirements. As such, we and our contract manufacturers 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. 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 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 or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA 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. 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, 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.

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 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 both 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 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 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. 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 at least one federal court has ruled is unconstitutional. 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 two percent per fiscal year, which went into effect in April 2013, and will remain in effect through 2024 unless additional Congressional action is taken. 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 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 Affordable Care Act's requirement that all Americans under age 65 have health insurance or pay a financial payment. 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.

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.

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 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 rebate), 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 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;

- 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. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which imposes 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, 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;

- the U.S. federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act," created under the Affordable Care Act, 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 Centers

for Medicare and Medicaid Services, information related to payments or other transfers of value made to physicians, other healthcare providers, and teaching hospitals, as well as ownership and investment interests held by physicians, other healthcare providers, and their immediate family members;

- 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;
- 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.

As of May 25, 2018, the General Data Protection Regulation ("GDPR") regulates the collection and use of personal data in the EU. The GDPR covers any business, regardless of its location, that provides goods or services to residents in the EU and, thus, could incorporate our activities in EU member states. The GDPR imposes strict requirements on controllers and processors of personal data, including special protections for "sensitive information," which includes health and genetic information of individuals residing in the EU. GDPR grants individuals the opportunity to object to the processing of their personal information, allows them to request deletion of personal information in certain circumstances, and provides the individual with an express right to seek legal remedies in the event the individual believes his or her rights have been violated. Further, the GDPR imposes strict rules on the transfer of personal data out of the EU to regions that have not been deemed to offer "adequate" privacy protections, such as the U.S. currently. Failure to comply with the requirements of the GDPR and the related national data protection laws of the EU member states, which may deviate slightly from the GDPR, may result in warning letters, mandatory audits and financial penalties, including fines of up to four percent of global revenues, or 20,000,000 Euro, whichever is greater. As a result of the implementation of the GDPR, we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules.

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There is significant uncertainty related to the manner in which data protection authorities will seek to enforce compliance with GDPR. For example, it is unclear whether the authorities will conduct random audits of companies doing business in the EU, or act solely after complaints are filed claiming a violation of the GDPR. The lack of compliance standards and precedent, enforcement uncertainty and the costs associated with ensuring GDPR compliance may be onerous and adversely affect our business, financial condition, results of operations and prospects.

The increasingly global nature of our business operations 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.

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. 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.

In the event we conduct clinical trials in the European Economic Area ("EEA"), we may be subject to additional privacy laws. The GDPR became effective on May 25, 2018 and deals with the processing of personal data and on the free movement of such data. The GDPR imposes a broad range of strict requirements on companies subject to the GDPR, including requirements relating to having legal bases for processing personal information relating to identifiable individuals and transferring such information outside the EEA, including to the U.S., providing details to those individuals regarding the processing of their personal information, keeping personal information secure, having data processing agreements with third parties who process personal information, responding to individuals' requests to exercise their rights in respect of their personal information, 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. The GDPR increases substantially the penalties to which we could be subject in the event of any non-compliance, including fines of up to 10,000,000 Euros or up to two percent of our total worldwide annual turnover for certain comparatively minor offenses, or up to 20,000,000 Euros or up to four percent of our total worldwide annual turnover for more serious offenses. Given the new law, 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 new law.

In particular, national laws of member states of the EU are in the process of being adapted to the requirements under the GDPR, thereby implementing national laws which may partially deviate from the GDPR and impose different obligations from country to country, so that we do not expect to operate in a uniform legal landscape in the EU. Also, as it relates to processing and transfer of 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.

In the event we conduct clinical trials in the EEA, we must also ensure that we maintain adequate safeguards to enable the transfer of personal data outside of the EEA, in particular to the U.S., in compliance with European data protection laws. We expect that we will continue to face uncertainty as to whether our efforts to comply with our obligations under European privacy laws 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 the Company.

Risks Related to Our 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 our 2014 license agreement with Caribou (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, Caribou has challenged the scope of our licensed rights and fields under our license agreement, which could adversely impact our exclusive rights to use CRISPR/Cas9 technology in our human therapeutics field. On October 17, 2018, we initiated an arbitration proceeding against Caribou asserting that it 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 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, purportedly invented or controlled by Caribou, in our exclusive human therapeutic field. Under the Caribou License, Caribou granted to the Company a worldwide, exclusive license to all of Caribou's intellectual property relating to CRISPR/Cas9 technology for all therapeutic, prophylactic and palliative uses and applications for any or all diseases and conditions in humans with the sole exceptions of anti-microbial and/or anti-fungal applications. The license encompassed all CRISPR/Cas9 intellectual property developed or controlled by Caribou as of July 16, 2014 and through an intellectual property cutoff date (January 30, 2018) that was necessary or useful for us to develop, manufacture or commercialize products in our field, as well as any technology developed by Caribou under a service agreement entered into by the Company and Caribou in July 2014. Caribou has asserted that the two families of intellectual property are outside the scope of our license, and that the scope of our human therapeutics field does not prevent it from developing and commercializing competing therapies. In accordance with the Caribou License, we initiated an arbitration seeking a declaration that the disputed intellectual property is included within the scope of our license under the Caribou License, an award of compensatory, consequential and punitive damages based on Caribou's conduct, and an injunction prohibiting Caribou from licensing or using this intellectual property in our exclusive human therapeutics field, among other claims. If we were not to succeed in this arbitration, it is possible that Caribou could use CRISPR/Cas9 to develop therapeutic, prophylactic and palliative uses and applications for diseases and conditions in humans in any field.

In addition, third parties could assert that UC/Vienna/Charpentier do not have rights to the CRISPR/Cas9 technology, or that any rights owned by UC/Vienna/Charpentier are limited. For example, 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 (collectively, the "Broad Institute patent family") that also claim certain aspects of CRISPR/Cas9 systems to edit genes in eukaryotic cells, including human cells. Because the respective owners of a UC/Vienna/Charpentier patent application 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. In January 2016, an interference proceeding was declared in the U.S. Patent and Trademark Office ("USPTO") between the claims from one UC/Vienna/Charpentier patent application we sublicense through Caribou (which generally claimed methods to use the CRISPR/Cas9 technology with a single RNA guide in any cellular or non-cellular setting) and certain U.S. patents and one application of the Broad Institute patent family (which generally claimed methods to use the CRISPR/Cas9 technology in eukaryotic cells). The interference proceeding was initiated to determine which set of inventors invented first and, thus, is entitled to patents on the invention in the U.S. In February 2017, the Patent Trial and Appeal Board ("PTAB") dismissed the interference proceeding finding that the respective patent claims involved in the interference were legally distinct such that they did not meet the legal requirement to proceed with the interference. The PTAB did not make any decision regarding inventorship or priority, and therefore

ownership, of the inventions claimed by the patents and applications at issue. UC/Vienna/Charpentier appealed to the U.S. Court of Appeals for the Federal Circuit (the "Federal Circuit") seeking a review and reversal of the PTAB's decision to terminate the interference. On September 10, 2018, the Federal Circuit affirmed the PTAB's decision to terminate the interference proceeding. The time for UC/Vienna/Charpentier to ask for a rehearing by the Federal Circuit or permission to appeal from the U.S. Supreme Court has expired. The Federal Circuit returned the UC/Vienna/Charpentier allowable patent claims to the USPTO, and on April 23, 2019, the USPTO issued the patent covering generally the use of the CRISPR/Cas9 technology using a single RNA guide in any setting, including cellular settings. The USPTO is currently considering whether to declare one or more subsequent interferences between other UC/Vienna/Charpentier applications and some or all of the Broad patents involved in the terminated interference that claim the use of the CRISPR/Cas9 technology in eukaryotic cells or compositions of single guide RNAs. 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 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 UC/Vienna/Charpentier are unable to prevail in their inventorship claims or if the scope of their claims is narrowed 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.

Intellectual property owned by third parties 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 January 11, 2016, the PTAB declared an interference proceeding between certain patents and a patent application of the Broad Institute patent family and one UC/Vienna/Charpentier patent application to determine, based on priority of invention, whether the contested inventions belong either to UC/Vienna/Charpentier or to the Broad Institute in the U.S. This interference proceeding was discontinued by the PTAB in February 2017 without any finding regarding inventorship or priority. In discontinuing the interference proceeding, the PTAB found that the claim sets presented by the two parties were "patentably distinct" from each other and, thus, did not meet the statutory requirements for continuing the proceeding. In April 2017, UC/Vienna/Charpentier appealed to the U.S. Court of Appeals for the Federal Circuit seeking a review and reversal of the PTAB's decision to terminate the interference. On September 10, 2018, the Federal Circuit issued a ruling affirming the PTAB's decision to terminate the interference proceeding. The time for UC/Vienna/Charpentier to ask for a rehearing by the Federal Circuit or permission to appeal from the U.S. Supreme Court has expired. The Federal Circuit returned the UC/Vienna/Charpentier allowable patent claims to the USPTO, and on April 23, 2019, the USPTO issued a patent covering generally the use of the CRISPR/Cas9 technology using a single RNA guide in any setting, including cellular settings. In addition, UC/Vienna/Charpentier continues to prosecute other patent claims covering the CRISPR/Cas9 inventions, which could also result in allowable or issued patents in the U.S. Certain of the claims being prosecuted by UC/Vienna/Charpentier, if found allowable by the USPTO, could lead to interference proceedings against patents or patent applications owned by other parties, including the Broad Institute patent family, with respect to certain claims expressly relating to the use of CRISPR/Cas9 in eukaryotic cells. As of April 30, 2019, the USPTO has found certain patent applications in the UC/Vienna/Charpentier patent family allowable but for potentially interfering subject matter with a number of patent applications and/or certain patents issued to the Broad, which claim aspects of CRISPR/Cas9 systems and methods to edit genes in eukaryotic cells, including human cells, as well as single-guide RNA compositions. The PTAB has not yet declared an interference involving any of these applications. There is no specified deadline for the PTAB to act on these matters, and we cannot predict if or when they will act, and whether they will declare any interference. Further, the effects that any such results may have on us and our intellectual property position, including whether UC/Vienna/Charpentier will ultimately be successful in prosecuting to the issuance of a patent covering the CRISPR/Cas9 system that we are able to use under our license agreement with Caribou, are currently unknown. 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 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 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 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 and Novartis. 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.

On October 17, 2018, we initiated an arbitration proceeding against Caribou asserting that it is violating the Caribou License, as well as other contractual and legal rights, by using and seeking to license to third parties 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. Under the Caribou License, Caribou granted to the Company a worldwide, exclusive license to all of Caribou's intellectual property relating to CRISPR/Cas9 technology for all therapeutic, prophylactic and palliative uses and applications for any or all diseases and conditions in humans with the sole exceptions of anti-microbial and/or anti-fungal applications. The license encompassed all CRISPR/Cas9 intellectual property developed or controlled by Caribou as of July 16, 2014 and through an intellectual property cutoff date (January 30, 2018) that was necessary or useful for the Company to develop, manufacture or commercialize products in its field, as well as any technology developed by Caribou under a service agreement entered into by the Company and Caribou in July 2014. Caribou has asserted that the two families of intellectual property are outside the scope of our license, and that the scope of our human therapeutics field does not prevent it from developing and commercializing competing therapies. In accordance with the Caribou License, we have submitted a demand for arbitration seeking a declaration that the disputed intellectual property is included within the scope of our license under the Caribou License, an award of compensatory, consequential and punitive damages based on Caribou's conduct, and an injunction prohibiting Caribou from licensing or using this intellectual property in our exclusive human therapeutics field, among other claims. If we were not to succeed in this arbitration, it is possible

that Caribou could use CRISPR/Cas9 to develop therapeutic, prophylactic and palliative uses and applications for diseases and conditions in humans in any field.

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

- the scope of rights, if any, granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology, products and processes infringe on, or derive from, intellectual property of the licensor that is not subject to the license agreement;

- whether our licensor or its licensor had the right to grant the license agreement, or whether they are compliant with their contractual obligations to their respective licensor(s);
- whether third parties are entitled to compensation or equitable relief, such as an injunction, for our use of the intellectual property without their authorization;
- our right to sublicense patent and other rights to third parties, including those under collaborative development relationships;
- whether we are complying with our obligations with respect to the use of the licensed technology in relation to our development and commercialization of product candidates;
- our involvement in the prosecution, defense and enforcement of the licensed patents and our licensors' overall patent strategy;
- the allocation of ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and by us and our partners; and
- the amounts of royalties, milestones or other payments due under the license agreement.

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

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

Patents relating to our product candidates are controlled by certain of our licensors or their respective licensors. Each of our licensors or their licensors generally has rights to file, prosecute, maintain and defend the patents we have licensed from such licensor. If these licensors or any future licensees and in some cases, co-owners from which we do not yet have licenses, having rights to file, prosecute, maintain, and defend our patent rights fail to adequately conduct these activities for patents or patent applications covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using or selling competing products. We cannot be certain that such activities by our licensors or their respective licensors have been or will be conducted in compliance with applicable laws and regulations or in our best interests, or will result in valid and enforceable patents or other intellectual property rights. Pursuant to the terms of the license agreements with our licensors, the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and, even if we are permitted to pursue such enforcement or defense, we cannot ensure the cooperation of our licensors or, in some cases, other necessary parties, such as the co-owners of the intellectual property from which we have not yet obtained a license. We cannot be certain that our licensors or their licensors, and in some cases, their respective co-owners, will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. For example, with respect to our sublicensed rights from Caribou to UC/Vienna/Charpentier intellectual property, UC retained the right to control the prosecution, enforcement and defense of this intellectual property in its license agreement with Caribou and, pursuant to an Invention Management Agreement, shares these responsibilities with CRISPR Therapeutics 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. 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. 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 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, and reexamination 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.

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.

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

Proprietary Information may include information or material which has not been made generally available to the public, such as: (a) corporate information, including plans, strategies, methods, policies, resolutions, contractual negotiations or legal proceedings; (b) marketing information, including strategies, methods, customer identities or other information about customers, prospect identities or other information about prospects, or market analyses or projections; (c) financial information, including cost and performance data, debt arrangements, equity structure, investors and holdings, purchasing and sales data and price lists; (d) operational and technological information, including plans, specifications, manuals, forms, templates, software, designs, methods, procedures, formulas, discoveries, inventions, improvements, concepts and ideas; and (e) personnel information, including personnel lists, reporting or organizational structure, resumes, personnel data, compensation structure, performance evaluations and termination arrangements or documents.

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, which could include generally our corporate plans, strategies and agreements, financial information, personnel information and operational and technological information, including know-how that is not patentable or that we elect not to patent. 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 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 October 17, 2018, we initiated an arbitration proceeding against Caribou asserting that it is violating the Caribou License, as well as other contractual and legal rights, by using and seeking to license to third parties 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. In accordance with the Caribou License, we have submitted a demand for arbitration seeking a declaration that the disputed intellectual property is included within the scope of our license under the Caribou License, an award of compensatory, consequential, and punitive damages based on Caribou's conduct, and an injunction prohibiting Caribou from licensing or using this intellectual property in our exclusive human therapeutics field, among other claims. If we were not to succeed in this arbitration, it is possible that Caribou could use CRISPR/Cas9 to develop therapeutic, prophylactic and palliative uses and applications for diseases and conditions in humans in any field.

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. Such a loss of patent protection could have a material adverse impact on our business.

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.

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.

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 and Regeneron, 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.

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 Our Common Stock

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 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.

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 March 31, 2019, our executive officers, directors, five percent or greater stockholders and their affiliates beneficially own approximately 56.2 percent 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.

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.

The Company 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 offering in November 2017. 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 the Company’s 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 “Shelf Registration Statement”) with the SEC, in relation to the registration of common stock, preferred stock, warrants and/or 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 “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 Shelf Registration Statement and subject to the limitations thereof. The Company will pay to the Sales Agent cash commissions of 3.0 percent of the gross proceeds of sales of common stock under the Sales Agreement. As of March 31, 2019, approximately $66.3 million in shares of common stock remain eligible for sale under the Sales Agreement. Sales of common stock, convertible securities or other equity securities by us or our stockholders under the Shelf Registration Statement may represent a significant percentage of our common stock currently outstanding. If we or our stockholders sell, or the market perceives that we or our stockholders intend to sell, substantial amounts of our common stock under the Shelf Registration Statement or otherwise, the market price of our common stock could decline significantly.

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.

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 provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all 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 provides that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the 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 choice of 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 choice of forum provision contained in our certificate of incorporation 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.

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

As a public company, and particularly after 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. However, while we remained an emerging growth company, we were not required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. Under the statute, we ceased to be an emerging growth company on the date that is the earliest of: (i) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (ii) December 31, 2020; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC. We became a large accelerated filer for the fiscal year ending December 31, 2019, and as such we lost emerging growth status on December 31, 2018. To achieve compliance with Section 404 within the prescribed period, we engaged in a process to document and evaluate our internal control over financial reporting, which has been both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially 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. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Commencing December 31, 2018, we are no longer an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth companies no longer apply to us.

As of June 30, 2018, the market value of our common stock that was held by non-affiliates exceeded $700 million, so we no longer qualify for emerging growth company status commencing December 31, 2018. As a large-accelerated filer, we are now subject to certain disclosure requirements that are applicable to other public companies that were not been applicable to us as an emerging growth company. These requirements include:

- compliance with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- compliance with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements;
- full disclosure obligations regarding executive compensation; and
- compliance with the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

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 the Company, 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 the Company 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.

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 the Company’s 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.

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 the Company was founded in 2014, many such changes have been made and changes are likely to continue to occur in the future. For example, in December 2017, the U.S. president signed into law the TCJA that significantly reforms the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards ("NOLs"), allows for the expensing of capital expenditures, and effectuates the migration from a "worldwide" system of taxation to a territorial system. Our net deferred tax assets and liabilities were revalued in December 2017 at the then newly enacted U.S. corporate rate. We continue to examine the impact this tax reform legislation may have on our business. 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 shareholders' 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, 2018, we had federal and state NOLs of $128.2 million and $117.0 million, respectively, which begin to expire in 2034. As of December 31, 2018, we had federal and state research and development tax credit carryforwards of approximately $7.5 million and $4.8 million, which begin to expire in 2034 and 2030, respectively. Our net deferred tax assets and liabilities have been revalued at the newly enacted U.S. corporate rate. 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. Under the TCJA, net operating losses generated 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.

10.1	First Amendment to Lease, dated as of April 5, 2019, by and between the Company and MIT 130 Brookline Leasehold LLC. (1)
31.1	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. (1)
31.2	Certification of the Chief Financial Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. (1)
32.1	Certifications pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of The Sarbanes-Oxley Act of 2002, by John M. Leonard, M.D., President and Chief Executive Officer of the Company, and Glenn Goddard, Executive Vice President, Chief Financial Officer of the Company. (2)
101.INS	XBRL Instance Document.
101.SCH	XBRL Taxonomy Extension Schema Document.
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.

(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: May 2, 2019

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)