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: