Intellia Therapeutics, Inc.
Form 10-Q
October 31, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-Q

QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the quarterly period ended September 30, 2018

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 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 Exchange Act). Yes No

The number of shares outstanding of the registrant’s common stock as of October 26, 2018: 43,419,303 shares.

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PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

INTELLIA THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS (UNAUDITED)

(Amounts in thousands except share and per share data)

	September 30, 2018	December 31, 2017
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 293,248	$ 340,678
Accounts receivable	2,813	10,471
Prepaid expenses and other current assets	2,768	3,681
Total current assets	298,829	354,830
Property and equipment, net	16,935	15,272
Other assets	5,469	6,133
Total Assets	$ 321,233	$ 376,235
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$ 1,754	$ 2,172
Accrued expenses	9,893	7,999
Current portion of deferred revenue	14,268	21,188
Total current liabilities	25,915	31,359
Deferred revenue, net of current portion	31,996	44,111
Other long-term liabilities	52	168
Commitments and contingencies		
Stockholders' Equity:		
Common stock, $0.0001 par value; 120,000,000 shares authorized, 43,369,323 shares and 42,384,623 shares issued and outstanding, respectively	4	4
Additional paid-in capital	445,225	421,706
Accumulated deficit	(181,959)	(121,113)
Total stockholders' equity	263,270	300,597
Total Liabilities and Stockholders' Equity	$ 321,233	$ 376,235

See notes to consolidated financial statements.

INTELLIA THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS (UNAUDITED)

(Amounts in thousands except per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Collaboration revenue	$7,408	$7,317	$22,554	$19,449
Operating expenses:				
Research and development	23,237	17,481	69,197	46,477
General and administrative	8,270	5,711	23,481	17,812
Total operating expenses	31,507	23,192	92,678	64,289
Operating loss	(24,099)	(15,875)	(70,124)	(44,840)
Interest income	1,397	519	3,847	1,260
Net loss	$(22,702)	$(15,356)	$(66,277)	$(43,580)
Net loss per share, basic and diluted	$(0.53)	$(0.44)	$(1.55)	$(1.25)
Weighted average shares outstanding, basic and diluted	43,161	35,189	42,684	34,945

See notes to consolidated financial statements.

INTELLIA THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS (UNAUDITED)

(Amounts in thousands)

	Nine Months Ended September 30,	
	2018	2017
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$(66,277)	$(43,580)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	3,237	2,161
(Gain) Loss on disposal of property and equipment	(16)	112
Equity-based compensation	13,464	8,726
Changes in operating assets and liabilities:		
Accounts receivable	7,658	1,961
Prepaid expenses and other current assets	913	(508)
Accounts payable	(65)	(232)
Accrued expenses	1,423	302
Deferred revenue	(13,604)	(13,298)
Other assets	664	478
Other long-term liabilities	(116)	(92)
Net cash used in operating activities	(52,719)	(43,970)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	(4,766)	(7,694)
Net cash used in investing activities	(4,766)	(7,694)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from options exercised	9,457	508
Issuance of shares through employee stock purchase plan	598	356
Net cash provided by financing activities	10,055	864
Net decrease in cash and cash equivalents	(47,430)	(50,800)
Cash and cash equivalents, beginning of period	340,678	273,064
Cash and cash equivalents, end of period	$293,248	$222,264
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Purchases of property and equipment unpaid at period end	$922	$601

See notes to consolidated financial statements.

INTELLIA THERAPEUTICS, INC.

NOTES TO 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 proprietary, curative therapeutics utilizing a biological tool known as CRISPR/Cas9.

The 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 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 for the year ended December 31, 2017.

The unaudited 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. The only item comprising comprehensive loss is net loss.

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.

2. Summary of Significant Accounting Policies

Revenue Recognition

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2014-09, Revenue from Contracts with Customers (Topic 606), which superseded existing revenue recognition guidance. The Company adopted ASU 2014-09 and its related amendments (collectively known as "ASC 606") on January 1, 2018 using the modified retrospective method. The reported results for 2018 reflect the application of ASC 606 guidance while the reported results for 2017 were prepared under the guidance of ASC 605, Revenue Recognition ("ASC 605" or "legacy GAAP"). The adoption of ASC 606 represents a change in accounting principle that will more closely align revenue recognition with the delivery of the Company's goods and services and will provide financial statement readers with enhanced disclosures.

In accordance with 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:

1) Identify the contract with the customer

A contract with a customer exists when (i) the Company enters into an enforceable contract with a customer that defines each party's rights regarding the goods or services to be transferred and identifies the related payment terms, (ii) the contract has commercial substance, and (iii) 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. The Company applies judgment in determining the customer's intent and ability to pay, which is based on a variety of factors including the customer's historical payment experience, or in the case of a new customer, published credit and financial information pertaining to the customer.

2) Identify the performance obligations in the contract

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, whereby the customer can benefit from the good or service either on its own or together with other available resources, and are distinct in the context of the contract, whereby the transfer of the good or service is separately identifiable from other promises in the contract. To the extent a contract includes multiple promised goods and services, the Company must apply 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.

3) Determine the transaction price

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 September 30, 2018 contained a significant financing component.

4) Allocate the transaction price to performance obligations in the contract

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. However, if a series of distinct services that are substantially the same qualifies as a single performance obligation in a contract with variable consideration, the Company must determine if the variable consideration is attributable to the entire contract or to a specific part of the contract. 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.

5) Recognize revenue when or as the Company satisfies a performance obligation

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. Examples of control are using the asset to produce goods or services, enhance the value of other assets, or settle liabilities, and holding or selling the asset.

As of September 30, 2018, the Company's only revenue recognized is related to collaboration agreements with third parties. As discussed in further detail in Note 5, the Company enters into out-licensing agreements which are within the scope of ASC 606, under which it licenses certain rights to its product candidates to third parties. 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.

Licenses of intellectual property: If the license to the Company's intellectual property 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, and 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 performs its obligations under these arrangements.

The following table presents changes in the Company's contract liabilities during the nine months ended September 30, 2018 (in thousands):

	Balance at	Additions	Deductions	Balance at End of Period

	Beginning of Period			
Nine Months Ended September 30, 2018				
Contract liabilities:				
Deferred revenue	$ 59,868	$ 3,000	$ (16,604)	$ 46,264

During the nine months ended September 30, 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:	Nine Months Ended September 30, 2018
Amounts included in the contract liability at the beginning of the period	$ 16,604

The following tables show the impact of adoption to our consolidated statement of income and balance sheet (in thousands):

	Three Months Ended September 30, 2018		
	Impact of changes in accounting policies		
	As Reported	Balances without adoption of ASC 606	Effect of Change Higher/(Lower)
Collaboration revenue	$7,408	$7,103	$ 305
Operating loss	(24,099)	(24,404)	305
Net loss	$(22,702)	$(23,007)	$ 305
Net loss per share, basic and diluted	$(0.53)	$(0.53)	$ -

	Nine Months Ended September 30, 2018		
	Impact of changes in accounting policies		
	As Reported	Balances without adoption of ASC 606	Effect of Change Higher/(Lower)
Collaboration revenue	$22,554	$23,458	$ (904)
Operating loss	(70,124)	(69,220)	(904)
Net loss	$(66,277)	$(65,373)	$ (904)
Net loss per share, basic and diluted	$(1.55)	$(1.53)	$ (0.02)

	September 30, 2018		
	Impact of changes in accounting policies		
	As Reported	Balances without adoption of ASC 606	Effect of Change Higher/(Lower)
Liabilities:			
Deferred revenue - current	$14,268	$17,183	$ (2,915)
Deferred revenue - noncurrent	31,996	33,608	(1,612)
Stockholders' equity:			
Accumulated deficit	$(181,959)	$(186,486)	$ 4,527

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.

The Company has applied the new standard to all of its contracts as of January 1, 2018.

Recent Accounting Pronouncements

In May 2014, the FASB issued ASC 606, which superseded existing revenue recognition guidance. The standard's core principle is that a company will recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. The Company adopted ASC 606 effective on January 1, 2018 using the modified retrospective method. Please see the above "Revenue Recognition" section for a discussion of the Company's updated policies related to revenue recognition and accounting for costs to obtain and fulfill a customer contract.

Impact of Adoption

The Company adopted ASC 606 using the modified retrospective method. The cumulative effect of applying the new guidance to all contracts with customers that were not completed as of January 1, 2018 was recorded as an adjustment to accumulated deficit as of the adoption date. As a result of applying the modified retrospective method to adopt the new guidance, the following adjustments were made to accounts on the consolidated balance sheet as of January 1, 2018:

Consolidated Balance Sheet

	January 1, 2018 (in thousands)		
		ASC 606	
	Pre-Adoption	Adjustment	Post-Adoption
Current portion of deferred revenue	$21,188	$ (2,769)	$ 18,419
Deferred revenue, net of current portion	44,111	(2,662)	41,449
Accumulated deficit	(121,113)	5,431	(115,682)

In February 2016, the FASB issued ASU No. 2016-02, Leases (“ASU 2016-02”). ASU 2016-02 establishes Topic 842 which amends ASC 840, Leases, by introducing a lessee model that requires balance sheet recognition of most leases. Topic 842 was subsequently amended by ASU No. 2018-01, Land Easement Practical Expedient for Transition to Topic 842; ASU No. 2018-10, Codification Improvements to Topic 842, Leases; and ASU No. 2018-11, Targeted Improvements. The Company is the lessee under certain leases that are accounted for as operating leases. The proposed changes would require that substantially all of the Company’s operating leases be recognized as assets and liabilities on the Company’s balance sheet. ASU 2016-02 will be effective for the Company for annual periods, and interim periods within those annual periods, beginning January 1, 2019. The Company expects to adopt this new lease standard using the transition method made available by the FASB in ASU No. 2018-11, using the effective date of January 1, 2019 as our date of initial application. Using this transition method, the Company will recognize a cumulative effect adjustment to the opening balance of retained earnings on January 1, 2019. As a result of electing this method, disclosures required under the new standard will not be provided for dates or periods before January 1, 2019. Topic 842 provides several optional practical expedients in transition. The Company expects to elect the package of practical expedients which would mean the Company would not need to reassess its existing conclusions on lease identification, classification, and initial direct costs. The Company is still evaluating the election of the use-of-hindsight practical expedient. Additionally, Topic 842 allows practical expedients for ongoing accounting treatment. The Company expects to elect the short-term lease recognition exemption for all leases that qualify. This means for those leases that qualify, the Company would not recognize right-of-use (“ROU”) assets or lease liabilities. The Company also expects to elect the practical expedient which allows it not to separate lease and non-lease components for all its leases.

While the Company continues to assess the effects of adoption and cannot reasonably estimate the impact at this time, the Company does expect that this standard will have a material impact on its consolidated financial statements. The Company expects the most significant effects to be the recognition of both ROU assets and lease liabilities for our operating leases as well as significant new lease-related disclosures.

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 September 30, 2018 and December 31, 2017 consisted primarily of cash and cash equivalents, accounts receivable and accounts payable. As of September 30, 2018 and December 31, 2017, the Company's financial assets recognized at fair value on a recurring basis consisted of the following:

	Fair Value as of September 30, 2018			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	$289,723	$289,723	$ —	$ —
Total	$289,723	$289,723	$ —	$ —

	Fair Value as of December 31, 2017			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	$330,896	$330,896	$ —	$ —
Total	$330,896	$330,896	$ —	$ —

The Company estimates the fair value of its cash equivalents using quoted market prices in active markets. 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:

	September 30, 2018	December 31, 2017
	(In thousands)	
Employee compensation and benefits	$5,119	$ 4,773
Research and development and professional expenses	4,774	3,226
Accrued expenses	$9,893	$ 7,999

5. Collaborations

Novartis Institutes for BioMedical Research

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

("HSC"s).

Agreement Structure

Under the terms of the collaboration, the Company and Novartis may research potential therapeutic, prophylactic and palliative ex vivo applications of the CRISPR/Cas9 technology in HSCs and CAR-T cells. 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 last of which closes 90 days before the fifth anniversary of the effective date of the Novartis Agreement. 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. If Novartis does not exercise its selection rights within each selection window, any such rights will be deemed forfeited by Novartis. Novartis is required to use commercially reasonable efforts to research, develop and commercialize a specified number of HSC products directed to each of their selected HSC targets.

The Company also agreed to collaborate with Novartis on research activities for CAR-T cell targets pursuant to a CAR-T cell program research plan approved by the CAR-T cell subcommittee of the collaboration's joint steering committee. After completion of the activities contemplated by the CAR-T cell program research plan, Novartis will assume sole responsibility for developing any products arising from that research plan and will be responsible for additional 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 the last two years of the five-year collaboration term, Novartis will have 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 our 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.

The Company received an upfront technology access payment from Novartis of $10.0 million in January 2015 and is 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. For each product under the collaboration, 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 may also be eligible to receive payments for: (i) each additional HSC target selected by Novartis beyond its initial defined allocation, (ii) each in vivo target that Novartis selects and (iii) any exercise by Novartis of certain license options under the Novartis Agreement. Additionally, at the inception of the arrangement, Novartis invested $9.0 million to purchase the Company's Class A-1 and Class A-2 Preferred Units under a Unit Purchase Agreement (the "Unit Purchase Agreement"). The Company considered whether the Unit Purchase Agreement would be subject to combination with the Novartis Agreement and determined that they should be combined because the terms of these arrangements are closely interrelated and were negotiated contemporaneously. The Unit Purchase Agreement and the Novartis Agreement are collectively referred to herein as the "Novartis Arrangement".

The Company assessed the Novartis Arrangement in accordance with ASC 606. The Company evaluated the promised goods and services under the Novartis Arrangement and determined that the Novartis Arrangement 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.

Under the Novartis Arrangement, the Company determined that the transaction price 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.

Collaboration Revenue

Through September 30, 2018, 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 $37.4 million in cash and accounts receivable under the Novartis Arrangement. Through September 30, 2018, the Company has recognized $35.7 million of collaboration revenue, including $2.4 million and $7.2 million during the three and nine months ended September 30, 2018, respectively, and $2.4 million and $6.8 million during the three and nine months ended September 30, 2017, respectively, in the consolidated statements of operations related to this agreement. As of September 30, 2018, there was approximately $11.6 million of the aggregate transaction price remaining to be recognized, which will be recognized through December 2019.

As of September 30, 2018 and December 31, 2017, the Company had accounts receivable of $1.0 million and $6.0 million, respectively, and deferred revenue of $1.6 million and $11.2 million, respectively, related to this agreement. Amounts for 2018 are reflective of accounting under ASC 606 and amounts for 2017 are reflective of accounting under ASC 605 and therefore may not be comparable.

Regeneron Pharmaceuticals, Inc.

In April 2016, the Company entered into a license and collaboration agreement (the "Regeneron Agreement") with Regeneron Pharmaceuticals, Inc. ("Regeneron"). The agreement includes a product component to research, develop and commercialize CRISPR/Cas-based therapeutic products primarily focused on genome editing in the liver as well as a technology collaboration component, 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.

Agreement Structure

Under the terms of the collaboration, the Company and Regeneron have agreed to a target selection process, whereby Regeneron may obtain exclusive rights for up to 10 targets to be chosen by Regeneron during the collaboration term, subject to 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. At the inception of the agreement, Regeneron selected the first of its 10 targets, which is subject to a co-development and co-commercialization arrangement between the Company and Regeneron.

The Company retains the exclusive right to solely develop products for certain indications. During the 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 are subject to further co-development and co-commercialization arrangements at the Company's or Regeneron's option, as applicable, which either can exercise pursuant to defined conditions. In July 2018, the Company and Regeneron agreed to a form of

Co-Development and Co-Promotion Agreement that will be used as the basis for each co-development/co-promotion agreement directed to a target and, simultaneously, the Company and Regeneron entered into the co-development/co-promotion agreement directed to the first collaboration target, ATTR, for which the Company will be the clinical and commercial lead. In addition, subject to certain restrictions, Regeneron will be able to replace a limited number of targets with substitute targets upon the payment of a specified replacement fee, in which case exclusive rights to the replaced target revert to the Company. Regeneron's target selections are subject to certain additional restrictions, including that non-liver targets are not the subject of ongoing or planned research and development by the Company or are not the subject of a collaboration or pending collaboration with a third party.

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 liver targets, and Regeneron will be responsible for preclinical research and the conduct of clinical development, manufacturing and commercialization of products directed to each of its exclusive targets under the oversight of a joint steering committee. 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.

In connection with this collaboration, Regeneron agreed to purchase $50.0 million of the Company's common stock in a private placement under a Stock Purchase Agreement (the "Stock Purchase Agreement") concurrent with the Company's initial public offering, and the Company received a nonrefundable upfront payment of $75.0 million. In addition, the Company is 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 U.S. and ex-U.S. regulatory approvals, 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 are further subject to the Company's existing low- to mid-single-digit royalty obligations under a license agreement with Caribou Biosciences, Inc. ("Caribou"). In addition, Regeneron is obligated to fund 50.0 percent of the research and development costs for the transthyretin amyloidosis program, the first target selected by Regeneron, which is subject to a co-development and co-commercialization arrangement between the Company and Regeneron.

The Company considered whether the Stock Purchase Agreement would be subject to combination with the Regeneron Agreement and determined that they should be combined because the terms of these arrangements are closely interrelated and were negotiated contemporaneously. The Stock Purchase Agreement and the Regeneron Agreement are collectively referred to herein as the "Regeneron Arrangement".

The Company assessed the Regeneron Arrangement in accordance with ASC 606. The Company evaluated the promised goods and services under the Regeneron Arrangement and determined that the Regeneron Arrangement 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.

Under the Regeneron Arrangement, 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.

Collaboration Revenue

Through September 30, 2018, excluding the amounts allocated to Regeneron's purchase of common stock, the Company recorded a $75.0 million upfront payment and $10.5 million for research and development services under the Regeneron Arrangement. Through September 30, 2018, the Company has recognized $40.9 million of collaboration revenue, including $5.0 million and $15.4 million during the three and nine months ended September 30, 2018, respectively, and $4.9 million and $12.6 million in the three and nine months ended September 30, 2017, respectively, in the consolidated statements of operations related to this arrangement. As of September 30, 2018, there was approximately $44.6 million of the aggregate transaction price remaining to be recognized, which will be recognized ratably through April 2022.

As of September 30, 2018 and December 31, 2017, the Company had deferred revenue of $44.6 million and $54.1 million, respectively, and accounts receivable of $1.8 million and $4.5 million, respectively, related to this arrangement.

Agreement Termination Rights

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 or any of its affiliates institutes a patent challenge against the Company's CRISPR/Cas or certain other background patent rights. The Company may also 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 intellectual property 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.

6. Equity-Based Compensation

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
	(In thousands)			
Research and development	$2,591	$1,987	$7,617	$5,048
General and administrative	1,865	1,260	5,847	3,678
Total	$4,456	$3,247	$13,464	$8,726

Restricted Stock

The following table summarizes the Company's restricted stock activity for the nine months ended September 30, 2018:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Unvested restricted stock as of January 1, 2018	479,822	$ 0.90
Granted	86,250	22.98
Vested	(378,033)	0.79
Cancelled	(44,524)	8.48
Unvested restricted stock as of September 30, 2018	143,515	$ 12.13

As of September 30, 2018, there was $2.2 million of unrecognized equity-based compensation expense related to restricted stock that is expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 1.5 years.

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 $21.29 per option and $18.19 per option for those options granted during the three and nine months ended September 30, 2018, respectively, and $13.45 and $10.73 per option for those options granted during the three and nine months ended September 30, 2017, respectively. Key assumptions used to apply this pricing model were as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Risk-free interest rate	2.8%	1.9%	2.6%	1.9%
Expected life of options	6.0 years	6.0 years	5.5-6.25 years	6.0 years
Expected volatility of underlying stock	87.7%	95.4%	88.9%	93.0%
Expected dividend yield	0.0%	0.0%	0.0%	0.0%

The following is a summary of stock option activity for the nine months ended September 30, 2018:

	Number of Options	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Outstanding at January 1, 2018	4,705,448	$ 12.09		
Granted	1,076,731	24.43		
Exercised	(982,142)	9.63		
Forfeited and Expired	(547,529)	16.55		
Outstanding at September 30, 2018	4,252,508	$ 15.20	7.98	$ 57,432
Exercisable at September 30, 2018	1,616,167	$ 10.49	6.83	$ 29,419

As of September 30, 2018, there was $30.1 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 2.8 years.

7. 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 September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
	(In thousands)			
Net loss	$(22,702)	$(15,356)	$(66,277)	$(43,580)
Weighted average shares outstanding, basic and diluted	43,161	35,189	42,684	34,945
Net loss per share, basic and diluted	$(0.53)	$(0.44)	$(1.55)	$(1.25)

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

	Periods Ended September 30,	
	2018	2017
	(In thousands)	
Unvested restricted stock	144	766
Stock options	4,253	4,421
Total	4,397	5,187

8. Related Party Transactions

Caribou Therapeutics

In July 2014, the Company issued Caribou Therapeutics Holdco, LLC, a wholly-owned subsidiary of Caribou, 8,110,599 Junior Preferred Units. As a result of this and related transactions, Caribou owned 9.2% of the Company's voting interests as of June 30, 2018.

The Company recognized general and administrative expense of $0.1 million and $0.7 million during the three and nine months ended September 30, 2018, respectively, and $0.1 million and $0.6 million, respectively, during the three and nine months ended September 30, 2017, related to the Company's obligation to pay 30.0 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, the Company issued Novartis 4,761,905 Class A-1 Preferred Units and 2,666,666 Class A-2 Preferred Units. In August 2015, Novartis acquired 761,905 shares of the Company's Series B Preferred 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 and subsequent transactions, Novartis collectively owned 9.9% of the Company's voting interests as of June 30, 2018.

The Company recognized collaboration revenue of $2.4 million and $7.2 million during the three and nine months ended September 30, 2018, respectively, and $2.4 million and $6.8 million in the three and nine months ended September 30, 2017, respectively, in the consolidated statements of operations related to this agreement. As of September 30, 2018 and December 31, 2017, the Company had recorded accounts receivable of $1.0 million and $6.0 million, respectively, and deferred revenue of $1.6 million and $11.2 million, respectively, related to this collaboration. Refer to Note 5, Collaborations, for additional information regarding this collaboration agreement.

9.Subsequent Event

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.

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 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 product candidates;
- our ability to advance any product candidates into, and successfully complete, clinical studies, including clinical studies necessary for regulatory approval and commercialization;
- our ability to advance our genome editing and therapeutic delivery capabilities;
- the scope of protection, including patents and license rights, we are able to establish and maintain for intellectual property 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 regulatory requirements and guidance regarding preclinical and clinical studies for genome editing products;
- 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, 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 and intellectual property licenses and rights and the scope 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 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") was formed in 2014 and is a leading genome editin company focused on the development of proprietary, curative therapeutics utilizing a biological tool known as CRISPR/Cas9. We believe that the CRISPR/Cas9 technology has the potential to revolutionize treatment for genetic disease by permanently editing disease-associated genes or genetic material in the human body with a single treatment course, and via cell therapies that can replace a patient's diseased cells or by using engineered immune cells to better treat cancer and immunological diseases. We intend to leverage our leading scientific expertise, clinical development experience and intellectual property ("IP") position to unlock broad therapeutic applications of CRISPR/Cas9 genome editing and develop new therapeutic products.

Our management's discussion and analysis of our financial condition and results of operations are based upon our unaudited 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 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, 2017.

We commenced active operations in mid-2014, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical research and studies and evaluating a clinical path for our pipeline programs. To date, we have financed our operations primarily through our collaborations with Novartis Institutes for BioMedical Research, Inc., ("Novartis"), and Regeneron Pharmaceuticals, Inc., ("Regeneron"), convertible preferred stock financings, our initial public offering and concurrent private placements of our common stock, and a follow-on public offering. All of our revenue to date has been collaboration revenue. Since our inception and through September 30, 2018, we have raised an aggregate of approximately $519.2 million to fund our operations, of which $122.7 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 and $85.0 million was from the sale of convertible preferred stock.

We are building a full-spectrum genome editing company and believe our product focus, therapeutic discovery and development strength, delivery expertise and IP portfolio make us well-positioned to translate the potential of the CRISPR/Cas9 system into clinically meaningful genome editing-based therapeutics. To maximize our opportunity to rapidly develop clinically successful products, we are applying a balanced and synergistic approach with our in vivo

and ex vivo initial indications. Our approach is defined by four primary criteria: (i) the type of edit—knockout, repair or insertion; (ii) the delivery modality for and modularity of in vivo and ex vivo applications; (iii) the presence of established therapeutic endpoints; and (iv) the potential for the CRISPR/Cas9 system to provide therapeutic benefits when compared to existing therapeutic modalities. Our initial indications include in vivo programs focused on diseases attributable to genes expressed in the liver that have significant unmet medical needs – transthyretin amyloidosis ("ATTR"), which we are co-developing with Regeneron, alpha-1 antitrypsin deficiency ("AATD"), and inborn errors of metabolism, such as primary hyperoxaluria type 1 ("PH1"). For ex vivo applications, our wholly owned programs focus on next-generation, engineered cell therapy solutions that we expect will ultimately be allogeneic. Our other ex vivo programs partnered with Novartis use CRISPR/Cas9 to potentially create improved chimeric antigen receptor T cell ("CAR-T cell") therapy, as well as engineered hematopoietic stem cell ("HSC") product candidates.

In May 2018, we presented data from ongoing non-human primate ("NHP") studies that demonstrated liver genome editing after a single systemic administration of lipid nanoparticles ("LNP"s) containing CRISPR/Cas9 cargo and an associated 60 percent reduction of transthyretin ("TTR") protein, a level that has been associated with therapeutic effects in other treatment modalities in patients. Based on these data, we are conducting investigational new drug ("IND")-enabling activities for a therapeutic to treat ATTR. In October 2018, at the European Society of Gene and Cell Therapy ("ESGCT") meeting, we presented additional data from our NHP studies further demonstrating a high correlation between liver editing and reduction of TTR. We reported that liver editing rates of approximately 35 to 40 percent in NHPs achieved a TTR protein reduction of greater than 60 percent, which is believed to be a therapeutically meaningful reduction of TTR. We also observed durability of liver editing and reduction of circulating TTR in this species for over six months. The data also demonstrated the transient nature of Intellia's proprietary modular LNP delivery system, which was rapidly cleared from circulation, with all CRISPR/Cas9 components undetectable in blood and liver within five days of administration.

Subsequent to the studies detailed above, we have observed further substantial increases in liver editing and corresponding TTR reduction rates with the inclusion (both independently and in combination) of further modifications to our guide RNA ("gRNA"), Cas9 messenger RNA ("mRNA") and lipid chemistry. Certain improvements have demonstrated up to 78 percent (mean of 59 percent) liver editing with up to 96 percent (mean reduction of 78 percent) TTR reduction in NHPs. As a result of these observations, we are further investigating the possibility of incorporating one or more of these improvements into our ongoing IND-enabling activities, which would result in submission of the IND application for our lead indication, ATTR, in 2020 in lieu of 2019. We continue to evaluate all components of our therapeutic candidates (including gRNA, Cas9 mRNA and lipid chemistry) through single and repeat dose experiments in NHPs in order to optimize our proprietary LNP-CRISPR/Cas9 delivery system. Further, we also continue to conduct studies across multiple animal models and across multiple primary liver cells to maximize editing rates through repeat dosing and formulation optimization.

We have also demonstrated continued progression of our modular LNP delivery platform capability to knock out various liver targets of interest in mice, including SERPINA1 for liver dysfunction associated with AATD and HAO1 for PH1. The most common genetic form of AATD is caused by a mutation in the SERPINA1 gene, that could manifest deleterious gain-of-function effects in the liver earlier in life as well as loss-of-function effects in the lung later in life in patients. Therefore, knocking out SERPINA1 could form the basis of a therapeutic for AATD-associated liver dysfunction. To date, we have achieved 85 percent editing of SERPINA1 in a mouse having the human SERPINA1 gene leading to an approximately 95 percent reduction of the encoded alpha1-antitrypsin ("AAT") protein. In PH1, excess oxalate produced in the liver, a condition called hyperoxaluria, crystallizes and accumulates in various organs and eventually causes kidney failure. Our therapeutic approach is to knock out genes involved in the metabolic pathway for oxalate production, including the gene HAO1, and thereby reduce the levels of glyoxylate and in turn urinary oxalate. In a mouse model of hyperoxaluria, we achieved approximately 80 percent editing of HAO1, leading to an approximately 45 percent reduction in urinary oxalate after a single dose. And, we also have observed up to 90 percent reduction in the protein expressed by HAO1 in a wild type mouse. These successful levels of editing reinforce the modular nature of our LNP delivery platform, including efficient and effective delivery to hepatocytes.

In October 2018, at ESGCT, we also reported our progress in advancing complex (insertion or repair) genome editing capabilities. In our collaboration with Regeneron, we combined our modular LNP delivery system of CRISPR/Cas9 with our proprietary modular adeno-associated viral ("AAV") insertion template to achieve supratherapeutic levels (levels higher than those required in a clinical setting) of gene expression in mice. Using F9, the gene encoding Factor

IX (“FIX”), as a model gene, we demonstrated the first robust, efficient CRISPR-mediated targeted insertion into the liver. FIX is a blood-clotting protein that is missing or defective in hemophilia B patients. Using our proprietary bi-directional template, we detected hybrid mAlb-hF9 transcripts in over 50 percent of hepatocyte cells following a single dose and achieved circulating human FIX protein levels of over 30,000 ng/mL. We observed that by varying either the LNP or the AAV doses, we could modulate FIX levels, while still maintaining stable and ongoing expression levels in all cases throughout 12 weeks of observation. 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.

In October 2017, we presented data from an in vivo mouse study showing, after a single intracerebral injection, delivery to the brain with one of our proprietary LNP formulations as demonstrated by the expression of tdTomato protein. Additionally, we presented data from another in vivo mouse study showing genome editing in brain tissue following single intracerebral injections of several proprietary LNP formulations. Editing was assessed under various dosing regimens with six different proprietary LNP formulations following a single intracerebral injection targeting the striatum and cerebellum. Under these various conditions, a range of editing levels from less than 1 percent up to 28 percent were achieved in the striatal and cerebellar tissue. The injections were well tolerated and the mice did not display any behavioral changes post dosing. We continue to advance our application of CRISPR/Cas9 technology to the central nervous system, including through our collaboration with Beverly Davidson, Ph.D., of the Children's Hospital of Philadelphia, who shared promising LNP delivery of green fluorescent protein ("GFP") to the striatum of NHPs at the American Society of Gene and Cell Therapy conference in May 2018 and at ESGCT in October 2018.

In December 2017, we and our collaborator Novartis shared initial data from our research collaboration on genome-edited human HSCs. These data showed successful ex vivo editing of the erythroid specific enhancer region of BCL11A, a gene associated with ameliorating sickle cell disease, and the ability of these cells to steadily engraft in mice while maintaining their desired properties. Specifically, the data showed that greater than 80 percent target site modification in HSCs and progenitor CD34+ cells was achieved following electroporation of ribonucleoprotein ("RNP") composed of Cas9 protein and a gRNA selected for efficacy and potency. In addition, we demonstrated an approximately 40 percent reduction in BCL11A mRNA with a corresponding two-fold increase in -globin transcript and 30 to 40 percent more fetal hemoglobin-positive cells above background. Editing of CD34+ cells from patient donors resulted in similar decreases in BCL11A mRNA and increases in -globin transcript. We also showed engraftment over 16 weeks following transplantation of edited human bone marrow CD34+ cells into immune compromised mice, while maintaining editing levels in engrafted cells. We did not observe any off-target events in CD34+ cells edited with the selected gRNA, as measured by targeted next generation sequencing of sites identified through in silico prediction and based on an unbiased, genome-wide, oligo-insertion detection method.

In May 2018, we and our collaborator Ospedale San Raffaele ("OSR"), presented the first update on our joint discovery and development efforts on Wilms' Tumor 1 ("WT1")-specific transgenic T cell receptors ("TCR"s). In conjunction with this presentation, we announced that our first cell therapy target is an epitope of the tumor-overexpressed protein WT1, for the treatment of acute myeloid leukemia ("AML") and other potential hematological malignancies, as well as for solid tumors. We shared findings showing the generation, characterization and advancement of WT1-specific, transgenic T cells against multiple WT1 epitopes presented on HLA-A*02:01 and other Class I alleles. Initial data demonstrating both recognition and killing of AML cells also was presented.

At the ESGCT meeting in October 2018, we and our collaborator OSR shared an update on our progress with the presentation of in vitro data showing that CRISPR/Cas9 editing in T cells could achieve over 90 percent knockout of endogenous TCRs. In addition, we showed that, after insertion of WT1-specific TCRs, the engineered T cells were fully functional and capable of specifically killing approximately 40 percent of leukemic blasts that expressed WT1 antigen and the HLA-A*02:01 allele. We continue to develop engineered T cells for acute myeloid leukemia as part of our wholly owned ex vivo product pipeline based on these novel TCRs and our genome editing technology.

Collaborations

Novartis

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.

Agreement Structure

Under the terms of the collaboration, we and Novartis may research potential therapeutic, prophylactic and palliative ex vivo applications of our CRISPR/Cas9 technology in HSCs and CAR-T cells. We 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. We have the right to choose a limited number of HSC targets for our exclusive development and commercialization per the specified selection schedule. Following these selections by Novartis and us, 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 a specified number of HSC products directed to each of their selected HSC targets.

We have also agreed to collaborate with Novartis on research activities for CAR-T cell targets pursuant to the CAR-T cell program research plan approved by the CAR-T cell subcommittee of the collaboration's joint steering committee. After completion of the activities contemplated by the CAR-T cell program research plan, Novartis will assume sole responsibility for developing any products 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.

Starting in December 2017 and through the end of the collaboration in December 2019, Novartis has the option to select a limited number of targets for research, development and commercialization of in vivo therapies using our CRISPR/Cas9 platform, on a non-exclusive basis. Following Novartis' selection of each in vivo target, Novartis may offer us 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 us and Novartis. Novartis is required to use commercially reasonable efforts to research, develop and commercialize at least one in vivo product directed to each of its selected in vivo 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 us pursuant to our 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 us.

Under the agreement, we received an upfront technology access payment of $10.0 million and are 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. In addition, for each product under the collaboration, subject to certain conditions, we may be eligible to receive (i) up to $30.3 million in development milestones, including for the filing of an 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 the 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. We may also be eligible to receive payments for: (i) each additional HSC target selected by Novartis beyond its initial defined allocation, (ii) each in vivo target that Novartis selects and (iii) any exercise by Novartis of certain license options under the agreement. Additionally, at the inception of the arrangement, Novartis invested $9.0 million to purchase our 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.

Collaboration Revenue

Through September 30, 2018, excluding amounts allocated to Novartis' purchase of our Class A-1 and Class A-2 Preferred Units, we had recorded a total of $37.4 million in cash and accounts receivable under the Novartis agreement. Through September 30, 2018, we have recognized $35.7 million of collaboration revenue, including $2.4 million and $7.2 million during the three and nine months ended September 30, 2018, respectively, and $2.4 million and $6.8 million in the three and nine months ended September 30, 2017, respectively, in the consolidated statements of operations related to this agreement. As of September 30, 2018 and December 31, 2017, we had $0.1 million and $0.6 million of accounts receivable, respectively, and deferred revenue of $1.6 million and $11.2 million, respectively, related to this agreement.

Regeneron

In April 2016, we entered into a license and collaboration agreement with Regeneron. The agreement includes a product component to research, develop and commercialize CRISPR/Cas-based therapeutic products primarily focused on genome editing in the liver as well as a technology collaboration component, 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-based technology to enhance our genome editing platform. Under this agreement, we may access the Regeneron Genetics Center and proprietary mouse models to be provided by Regeneron for a limited number of our liver programs.

Agreement Structure

Under the terms of our collaboration, we and Regeneron have agreed to a target selection process, whereby Regeneron may obtain exclusive rights for up to 10 targets to be chosen by Regeneron during the collaboration term, subject to 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.

At the inception of the agreement, Regeneron selected the first of its 10 targets, which is subject to a co-development and co-commercialization arrangement between us and Regeneron. We retain the exclusive right to solely develop products for certain targets, including targets associated with the genetic diseases PH1 and AATD. During the target selection process, we have the right to choose additional liver targets for our own development using commercially reasonable efforts. Certain targets that either we or Regeneron select may be subject to further co-development and co-commercialization arrangements at our or Regeneron's option, as applicable, which either can exercise pursuant to defined conditions. In July 2018, we and Regeneron agreed to a form of Co-Development and Co-Promotion Agreement that will be used as the basis for each co-development/co-promotion agreement directed to a target and, simultaneously, we and Regeneron entered into the co-development/co-promotion agreement directed to the first collaboration target, ATTR, for which we will be the clinical and commercial lead. In addition, subject to certain restrictions, Regeneron will be able to replace a limited number of targets with substitute targets upon the payment of a specified replacement fee, in which case exclusive rights to the replaced target revert to us. Regeneron's target selections are subject to certain additional restrictions, including that non-liver targets are not the subject of ongoing or planned research and development by us or are not the subject of a collaboration or pending collaboration with a third party.

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. We will assist Regeneron with the preliminary evaluation of liver targets, and Regeneron will be responsible for preclinical research and the conduct of clinical development, manufacturing and commercialization of products directed to each of its exclusive targets under the oversight of a joint steering committee. We 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 initial 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.

In connection with this collaboration, Regeneron agreed to purchase $50.0 million of our common stock in a private placement concurrent with our initial public offering, and we received a nonrefundable upfront payment of $75.0 million. In addition, we are eligible to earn, on a per-licensed target basis, up to $25.0 million, $110.0 million and $185.0 million in development, regulatory and sales-based milestone payments, respectively. We are 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 are further subject to our existing low- to mid-single-digit royalty obligations under a license agreement with Caribou Biosciences, Inc. ("Caribou"). In addition, Regeneron is obligated to fund 50.0 percent of certain research and development costs for the TTR program, the first target selected by Regeneron, which is subject to a co-development and co-commercialization arrangement between us and Regeneron.

Collaboration Revenue

Through September 30, 2018, we recorded a $75.0 million upfront payment and $10.5 million for research and development services under the Regeneron agreement. Through September 30, 2018, we have recognized $40.9 million of collaboration revenue, including $5.0 million and $15.4 million during the three and nine months ended

September 30, 2018, respectively, and $4.9 million and $12.6 million during the three and nine months ended September 30, 2017, respectively, in the consolidated statements of operations related to this agreement. As of September 30, 2018 and December 31, 2017, we had deferred revenue of $44.6 million and $54.1 million, respectively, and accounts receivable of $1.8 million and $4.5 million, respectively, related to this agreement.

Results of Operations

Comparison of Three Months Ended September 30, 2018 and 2017

The following table summarizes our results of operations for the three months ended September 30, 2018 and 2017:

	Three Months Ended September 30,		
	2018	2017	Increase / (decrease)
	(In thousands)		
Collaboration revenue	$7,408	$7,317	$ 91
Operating expenses:			
Research and development	23,237	17,481	5,756
General and administrative	8,270	5,711	2,559
Total operating expenses	31,507	23,192	8,315
Operating loss	(24,099)	(15,875)	(8,224)
Interest income	1,397	519	878
Net loss	$(22,702)	$(15,356)	$ (7,346)

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.

Collaboration revenue increased to $7.4 million during the three months ended September 30, 2018, as compared to $7.3 million during the three months ended September 30, 2017. The increase in collaboration revenue during the quarter ended September 30, 2018 is primarily related to the recognition of amounts under the Regeneron collaboration. The specific Regeneron related increase is driven by increased research and development services related to our TTR program, increasing to $1.8 million during the three months ended September 30, 2018 as compared to $1.7 million during the three months ended September 30, 2017.

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, lab supplies and contract research services.

Research and development expenses increased $5.8 million to $23.2 million during the three months ended September 30, 2018, as compared to $17.5 million during the three months ended September 30, 2017. This increase is primarily

related to an increase in research and development expenses of $2.4 million related to laboratory supplies, research materials and services for the further advancement of our early-stage research programs; and an increase in personnel-related costs of $2.1 million, which includes equity-based compensation expense, driven by our growth in headcount.

Through 2018, we expect research and development expenses to increase as we continue to grow our research and development team and advance our research plans.

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. Other general and administrative expenses include 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.

General and administrative expenses increased $2.6 million to $8.3 million during the three months ended September 30, 2018, compared to $5.7 million during the three months ended September 30, 2017. This increase was primarily related to an increase of $1.5 million in personnel-related costs, which includes equity-based compensation expense, as we grew in headcount, as well as a $0.4 million increase in legal and other IP-related expense caused by the timing of these costs year over year.

Through 2018, 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 $0.9 million to $1.4 million during the three months ended September 30, 2018 as compared to $0.5 million during the three months ended September 30, 2017. This increase was caused by an increase in our average cash balance compared to the same period in the prior year, as well as a general increase in interest rates.

Interest income is income earned on our cash equivalents. The increase in interest income is due to the increase in interest-bearing money market accounts, commercial paper and U.S. treasury securities, as compared to the same period in the prior year.

Comparison of Nine Months Ended September 30, 2018 and 2017

The following table summarizes our results of operations for the nine months ended September 30, 2018 and 2017:

	Nine Months Ended September 30,		
	2018	2017	Increase / (decrease)
	(In thousands)		
Collaboration revenue	$22,554	$19,449	$ 3,105
Operating expenses:			
Research and development	69,197	46,477	22,720
General and administrative	23,481	17,812	5,669
Total operating expenses	92,678	64,289	28,389
Operating loss	(70,124)	(44,840)	(25,284)
Interest income	3,847	1,260	2,587
Net loss	$(66,277)	$(43,580)	$ (22,697)

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.

Collaboration revenue increased approximately $3.1 million to $22.6 million during the nine months ended September 30, 2018, as compared to $19.4 million during the nine months ended September 30, 2017. The increase in collaboration revenue during the nine months ended September 30, 2018 is primarily related to the recognition of amounts under the Regeneron collaboration. The specific Regeneron related increase is driven by increased research and development services related to our TTR program, increasing to $6.0 million during the nine months ended September 30, 2018 as compared to $3.2 million during the nine months ended September 30, 2017.

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, lab supplies and contract research services.

Research and development expenses increased $22.7 million to $69.2 million during the nine months ended September 30, 2018, as compared to $46.5 million during the nine months ended September 30, 2017. This increase is primarily related to an increase in research and development expenses of $11.7 million related to laboratory supplies, research materials and services for the further advancement of our early-stage research programs; an increase in personnel-related costs of $9.4 million, which includes equity-based compensation expense, driven by our growth in headcount; and $1.1 million in depreciation on lab equipment purchased during 2017 and early 2018.

Through 2018, we expect research and development expenses to increase as we continue to grow our research and development team and advance our research plans.

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. Other general and administrative expenses include 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.

General and administrative expenses increased $5.7 million to $23.5 million during the nine months ended September 30, 2018, compared to $17.8 million during the nine months ended September 30, 2017. This increase was primarily related to an increase of $4.7 million in personnel-related costs, which includes equity-based compensation expense, as we grew in headcount.

Through 2018, 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 $2.6 million to $3.8 million during the nine months ended September 30, 2018 as compared to $1.3 million during the nine months ended September 30, 2017. This increase was caused by an increase in our average cash balance compared to the same period in the prior year, as well as a general increase in interest rates.

Interest income is income earned on our cash equivalents. The increase in interest income is due to the increase in interest-bearing money market accounts, commercial paper and U.S. treasury securities, as compared to the same period in the prior year.

Liquidity and Capital Resources

Since our inception through September 30, 2018, we have raised an aggregate of $519.2 million to fund our operations, of which $122.7 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 and $85.0 million was from the sale of convertible preferred stock. As of September 30, 2018, we had $293.2 million in cash and cash equivalents.

In addition, we are entitled to receive technology access fees and 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.

On October 12, 2018, we 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"). We also simultaneously entered into an Open Market Sale Agreement (the "Sales Agreement") with Jefferies LLC, (the "Sales Agent"), to provide for the offering, issuance and sale by us of up to an aggregate amount of $100 million of our common stock from time to time in "at-the-market" offerings under the Shelf and subject to the limitations thereof. We shall pay to the sales agent cash commissions of 3.0 percent of the gross proceeds of sales of common stock under the Sales Agreement.

Funding Requirements

Our primary uses of capital are, and we expect will continue to be, research and development services, compensation and related expenses, laboratory and related supplies, legal and other regulatory expenses, patent prosecution filing and maintenance costs for our licensed IP and general overhead costs. During the next twelve months, we expect our expenses to increase compared to prior periods in connection with our ongoing activities, particularly as we continue research and development and preclinical activities.

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 technology access fees and research payments under our collaboration with Novartis. 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 and cash equivalents as of September 30, 2018, as well as technology access and research funding from Novartis and Regeneron, will enable us to fund our ongoing operating expenses and capital expenditures through mid-2020, 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 nine months ended September 30, 2018 and 2017:

	Nine Months Ended September 30,	
	2018	2017
	(In millions)	
Net cash used in operating activities	$(52.7)	$(44.0)
Net cash used in investing activities	(4.8)	(7.7)
Net cash provided by financing activities	10.1	0.9

Net cash used in operating activities

During the nine months ended September 30, 2018 and 2017, our operating activities used net cash of $52.7 million and $44.0 million, respectively. The use of net cash in both periods primarily resulted from our net losses and changes in our working capital accounts. The increase in net cash used in operations for the nine months ended September 30, 2018 as compared to the nine months ended September 30, 2017 was due primarily to higher operating expenses, driven by increased research and development activities and headcount, during the nine months ended September 30, 2018 of $92.7 million as compared to $64.3 million for the nine months September 30, 2017. These higher costs were offset in part by the receipt of cash from Novartis in both nine-month periods and receipts of cash from Regeneron of $8.6 million in the nine months ended September 30, 2018 as compared with receipts of cash of $0.1 million in the nine months ended September 30, 2017.

Net cash used in investing activities

During the nine months ended September 30, 2018 and 2017, our investing activities used net cash of $4.8 million and $7.7 million, respectively. The use of cash in both periods related to purchases of property and equipment as we grow our operations and build out our office and laboratory facilities. The decrease in the nine months ended September 30, 2018 as compared with the same period in 2017 is primarily due to purchases and build-out in early 2017 related to the move to our new corporate office in December 2016.

Net cash provided by financing activities

During the nine months ended September 30, 2018 and 2017, our net cash provided by financing activities was $10.1 million and $0.9 million, respectively. Net cash provided by financing activities during the nine months ended September 30, 2018 is made up of $9.5 million in cash received from the exercise of stock options and $0.6 million in cash received from the issuance of shares through our employee stock purchase plan. Net cash provided by financing activities during the nine months ended September 30, 2017 is made up of $0.5 million in cash received from the exercise of stock options and $0.4 million in cash received from the issuance of shares through our employee stock purchase plan.

Critical Accounting Policies

Our critical accounting policies require the most significant judgments and estimates in the preparation of our consolidated financial statements. Management has determined that our most critical accounting policies are those relating to revenue recognition and equity-based compensation. As discussed in Note 2 to our consolidated financial statements, we adopted Accounting Standards Update No. 2014-09, Revenue from Contracts with Customers (Topic 606) ("ASU 2014-09") effective January 1, 2018. 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, 2017.

Recent Accounting Pronouncements

Please read Note 2 to our consolidated financial statements included in Part I, Item 1, "Notes to Consolidated Financial Statements," of this quarterly report on Form 10-Q for a description of recent accounting pronouncements applicable to our business.

Contractual Obligations

There were no material changes to our contractual obligations during the nine months ended September 30, 2018. 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, 2017.

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 Securities and Exchange Commission.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of September 30, 2018, we had cash equivalents of $289.7 million consisting of interest-bearing money market accounts, commercial paper 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. Due to the short-term maturities of our cash equivalents and the low risk profile of these investments, we believe that we do not have any material exposure to changes in the fair value of our investment portfolio as a result of changes in interest rates. Declines in interest rates, however, would reduce future investment income.

We do not have any foreign currency or other derivative financial instruments, and we do not believe that inflation had a material effect on our results of operations during the nine months ended September 30, 2018. Inflation generally affects us by increasing our cost of labor and clinical trial costs.

Item 4. Controls and Procedures

Disclosure Controls and Procedures

The Company has established disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) 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 and accounting officer (our "Chief Financial Officer"), to allow timely decisions regarding required disclosure.

Our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Quarterly Report on Form 10-Q. Management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of September 30, 2018.

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 September 30, 2018 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, commercial arrangements and other matters, including the matters 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 against Caribou asserting that Caribou is violating the terms and conditions of the license agreement entered into by the Company and Caribou in July 2014 ("Caribou License"), as well as other contractual and legal rights, by using and seeking to license to third parties two patent families relating to specific structural or chemical modifications of guide RNAs, that were purportedly invented or controlled by Caribou, in our exclusive human therapeutic field. Under the Caribou License, Caribou granted to the Company a worldwide, exclusive license to all of Caribou's intellectual property relating to CRISPR/Cas9 technology for all therapeutic, prophylactic and palliative uses and applications for any or all diseases and conditions in humans, with the sole exceptions of anti-microbial and/or anti-fungal applications. The license encompassed all CRISPR/Cas9 intellectual property developed or controlled by Caribou as of July 16, 2014 and through an intellectual property cutoff date (January 30, 2018) that was necessary or useful for us to develop, manufacture or commercialize products in our field, as well as any technology developed by Caribou under a service agreement entered into by the Company and Caribou in July 2014. Caribou has asserted that the two families of intellectual property are outside the scope of our license. In accordance with the Caribou License, we have submitted a demand for arbitration seeking a declaration that the disputed intellectual property is included within the scope of our license under the Caribou License, an award of compensatory, consequential and punitive damages based on Caribou's conduct, and an injunction prohibiting Caribou from licensing or using this intellectual property in our exclusive human therapeutics field, among other claims.

University of California/University of Vienna/Charpentier Patent Interference

As reported in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, on April 13, 2015, UC/Vienna/Charpentier jointly filed a request with the United States Patent and Trademarks Office (the "USPTO") asking that an interference be declared between a UC/Vienna/Charpentier patent application and certain patents issued to the Broad Institute, Massachusetts Institute of Technology, the President and Fellows of Harvard College and Rockefeller University (collectively, the "Broad Institute patent family" or the "Broad"), which claim aspects of CRISPR/Cas9 systems and methods to edit genes in eukaryotic cells, including human cells. An interference is an adversarial proceeding to determine the initial inventor of a particular invention claimed in patents and patent applications owned by different parties. An interference is conducted by the USPTO's Patent Trial and Appeal Board (the "PTAB"). On January 11, 2016, the PTAB declared an interference involving one UC/Vienna/Charpentier application, 12 Broad issued patents and a Broad patent application. In the order declaring the interference, the PTAB designated UC/Vienna/Charpentier the "Senior Party" and the Broad the "Junior Party". In March 2016, the PTAB re-declared the interference to add an additional U.S. patent application owned by the Broad. On February 15, 2017, the PTAB dismissed the proceeding finding that the parties' respective patent claims involved in the interference were distinct such that they did not meet the legal requirement to proceed with the interference. Specifically, the PTAB

concluded that the Broad's claims were directed to the use of CRISPR/Cas9 only in eukaryotic cells and, thus were patently distinct from UC/Vienna/Charpentier's claims, which were directed to the use of CRISPR/Cas9 in all settings. As a result of this proceeding's dismissal, the PTAB did not make a decision regarding which party actually first invented the use of CRISPR/Cas9 systems and methods to edit genes in eukaryotic cells. In April 2017, UC/Vienna/Charpentier appealed to the U.S. Court of Appeals for the Federal Circuit seeking a review and reversal of the PTAB's decision. On September 10, 2018, the Federal Circuit affirmed the PTAB's decision to terminate the interference proceeding.

"Item 3. Legal Proceedings" of our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 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, 2017 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 Our Business, Technology and Industry

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 the fields of gene therapy, which typically involves introducing a copy of a gene into a patient's cell, 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-edited engineered cell therapy has been approved, and the potential to successfully do so 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 modify 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 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 initial 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, scalable or profitable in our selected indications or any other indication we pursue.

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, as well as applicable regulatory guidance for preclinical testing and clinical studies from the Food and Drug Administration ("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, 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 introduce or remove genetic information in vivo to treat various disorders, or to modify 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 and commercializing our product candidates subject us to a number of challenges, including:

- obtaining regulatory approval from the FDA and other regulatory authorities that have very limited or no experience with the clinical development of CRISPR/Cas9 therapeutics;
- 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, 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;
- 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 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 ex vivo CRISPR/Cas9-based therapeutics have been authorized in the U.S. and EU member states; and no company or research institution has been authorized to commence human clinical trials utilizing in vivo CRISPR/Cas9 therapies in the U.S. or the 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 EMA will apply to CRISPR/Cas9 product candidates the same regulatory pathway and requirements it is applying to other 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 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 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.

Further, 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 modernize 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 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 the timing and our ability to obtain approval for our products. 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 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.

Even if we obtain regulatory approval of any product candidates, such candidates may not gain market acceptance among physicians, patients, hospitals, third-party payors and others in the medical community.

The use of the CRISPR/Cas9 system as a framework for developing genome editing-based therapies is a recent development and may not become broadly accepted by physicians, patients, hospitals, third-party payors and others in the medical community. A variety of factors will influence whether our product candidates are accepted in the market, including, for example:

- the clinical indications for which our product candidates are approved;
- the potential and perceived advantages of our product candidates over alternative treatments;

- the incidence and severity of any side effects, including any unintended DNA changes;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA or other regulatory authorities;
- the timing of market introduction of our product candidates;
- availability or existence of competitive products;
- the cost of treatment in relation to alternative treatments;

- the amount of upfront costs or training required for health care providers to administer our product candidates;
- the availability of adequate coverage, reimbursement and pricing by third-party payors and government authorities;
- patients' ability to access physicians and medical centers capable of delivering any therapies that we develop;
- the willingness of patients to pay out of pocket in the absence of coverage and reimbursement by third-party payors and government authorities;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies;
- any restrictions on the use of our product candidates together with other medications;
- interactions of our product candidates with other medicines patients are taking;
- potential adverse events for any products developed, or negative interactions with regulatory agencies, by us or others in the gene therapy and genome editing fields; and
- the effectiveness of our sales and marketing efforts and distribution support.

Even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete. In addition, adverse publicity due to the ethical and social controversies surrounding the therapeutic in vivo use of CRISPR/Cas9, gene edited modified cells, or other therapeutics mediums, such as viral vectors that we may use in our clinical trials may limit market acceptance of our product candidates. If our product candidates are approved but fail to achieve market acceptance among physicians, patients, hospitals, third-party payors or others in the medical community, we will not be able to generate significant revenue.

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.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, if approved, which could make it difficult for us to sell any product candidates or therapies profitably.

The success of our product candidates, if approved, depends on the availability of adequate coverage and reimbursement from third-party payors, including government agencies. In addition, because our product candidates represent new approaches to the treatment of genetic-based diseases, we cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors are critical to new product acceptance.

Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

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

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

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

We intend to seek approval to market our product candidates in both the U.S. and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the EU, the pricing of pharmaceutical products, including biologics, is subject to governmental control and other market regulations which

could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future health care reform measures.

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, 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 TTR 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, 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;
- 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;
- 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;
- 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;
- a product candidate may not be capable of being produced in 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 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 factors.”

If we do not successfully develop 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.

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.

The reported results of our NHP studies may ultimately differ from future results as additional data are received and fully evaluated.

The reported results of the NHP studies that we have publicly disclosed, and that are discussed herein and in documents we incorporated by reference, consist of data from our ongoing and limited studies. These data were based on an analysis of the available data from an ongoing series of studies, and therefore the reported results, findings and conclusions related to these data are subject to change following further and more comprehensive review of the data or additional and new data that we expect to receive related to, or following up on, the studies. Our reported results and related data are based on assumptions, estimations, calculations and information available to us at the time we initially report the data. Results from subsequent studies may differ from, or be inconsistent with, the reported results, or different conclusions or considerations may qualify such results, once the current data or additional data have been received and further evaluated. Even once we validate the data, there is no assurance that we will be able to reproduce such data or generate improved data results in subsequent preclinical studies. In addition, third parties, including regulatory agencies, may not accept or agree with our assumptions, estimations, calculations or analyses, or may interpret or weigh the importance of data differently, which could impact the value of our technology, the approvability or commercialization of product candidates and our business in general. If the data that we have reported related to NHP differ from actual results or we are unable to reproduce similar or improved data in subsequent preclinical studies, our ability to develop, obtain approval for, and commercialize, our products may be harmed, which could harm our business, financial condition, operating results or prospects.

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 an 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;
-