2017 Annual Report

John Leonard, M.D.
President & Chief Executive Officer

To Our Shareholders:

A genomic medicine revolution is here and Intellia Therapeutics is at its forefront.

2017 was a remarkable year for our company in advancing genome editing technology and the development of new CRISPR/Cas9-based therapies. Our accomplishments and work focus on our mission of *developing curative genome editing treatments that can positively transform the lives of people living with severe and life-threatening diseases.* And they demonstrate that every employee at Intellia understands and is committed to our mission – we think courageously, push the boundaries, advance relentlessly and design solutions to advance scientific innovation. Consequently, we have made substantial progress in genetic disease research and development, and achieved the ambitious goals we set for our company last year.

With our partner Regeneron Pharmaceuticals, Inc., we made significant strides in our lead liver program focused on transthyretin amyloidosis, a rare genetic disorder where mutated transthyretin (TTR) genes result in toxic protein deposits in a patient's tissues, causing organ failure. In our preclinical studies, we successfully demonstrated knockout of the TTR gene in mice, rats and non-human primates, a critical requirement before initiating human clinical studies. Earlier in 2017, we demonstrated durable *in vivo* genome editing in mice over the course of one year, supporting the hypothesis that CRISPR/Cas9 can reach and edit liver stem cells. Based on these accomplishments, we are moving ahead with investigational new drug enabling activities in mid-2018 to cure transthyretin amyloidosis.

In addition, we progressed our genome editing platform to address alpha-1 antitrypsin deficiency, a serious rare disorder that attacks the lungs and liver, and showed promising knockout editing in mice of the mutated SERPINA1 gene that gives rise to liver complications in certain patients. As we build on this success, we have the potential to achieve insertion/repair goals in our alpha-1 clinical studies.

Moreover, we advanced the *in vivo* application of our CRISPR/Cas9 technology to more complex edits in the liver and other organs. With our partner Regeneron, we demonstrated successful insertion of template DNA coding sequence and achieved therapeutically relevant levels of gene expression in mice, representing a key step in accomplishing more complex editing. This is a major advance in the genome editing field as we expand the technology to address diseases that require genetic restoration.

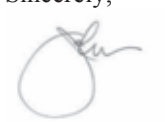
In parallel with the momentum in our *in vivo* programs, we continued to develop our *ex vivo* cell therapy efforts. With one of our partners in this area, the Novartis Institutes for Biomedical Research, we recently presented data showing clinically significant editing of cells to levels sufficient to address sickle cell disease, and that those cells retained normal genetic function when re-introduced into mice.

I'm proud of the talent we have brought together at Intellia, and of our scientific, manufacturing and support capabilities. Following our public offering in November that successfully raised $150 million in capital, we will augment the resources needed to execute on our current programs as we prepare to enter the clinic with our first product candidate and further expand our research pipeline.

Our 2017 accomplishments set the stage for continued success. In 2018, we will focus on carrying out activities and studies to support our TTR program, proceed with other liver indications in non-human primate studies, advance our *in vivo* preclinical work in a second organ, and expand our proprietary *ex vivo* programs in immuno-oncology and autoimmunity.

Our culture, strategy and focus on execution are a potent mix for success at Intellia. They guide the commitments we've made to shareholders and patients. Our 2018 goals focus on the path to the clinic so we can deliver CRISPR/Cas9 therapies to the patients we hope to serve. At Intellia, we never forget that patients are counting on us to make the potential of genome editing therapy a reality.

Sincerely,



UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2017

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

For the transition period from _____ to _____

Commission File Number 001-37766

INTELLIA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**36-4785571**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
40 Erie Street, Suite 130 Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	**(Zip Code)**

(857) 285-6200
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.0001 par value per share	**Nasdaq Global Market**

Securities registered pursuant to Section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒ (Do not check if a smaller reporting company)	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 aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $235.3 million as of June 30, 2017 (based on a closing price of $16.00 per share as quoted by the Nasdaq Global Market as of such date). In determining the market value of non-affiliate common stock, shares of the registrant's common stock beneficially owned by officers, directors and affiliates have been excluded. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The registrant had 42,387,435 shares of Common Stock, $0.0001 par value per share, outstanding as of February 28, 2018.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report on Form 10-K incorporates by reference certain information from the registrant's definitive Proxy Statement for its 2018 annual meeting of shareholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year end of December 31, 2017. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as part of this Form 10-K.

Intellia Therapeutics, Inc.
Annual Report on Form 10-K for the Fiscal Year Ended December 31, 2017

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Forward-looking Information

This Annual Report on Form 10-K contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements may be identified by such forward-looking terminology as "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. Our forward-looking statements are based on a series of expectations, assumptions, estimates and projections about our company, are not guarantees of future results or performance and involve substantial risks and uncertainty. We may not actually achieve the plans, intentions or expectations disclosed in our 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;*
- *our ability to apply a risk-mitigated strategy to efficiently discover and develop product candidates, including by applying learnings from one program to other programs;*
- *our ability to create 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;*
- *our ability to advance our therapeutic delivery capabilities;*
- *the scope of protection 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 the proprietary rights of others;*
- *the issuance of regulatory 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 licenses or obtain additional funding;*
- *our financial performance;*
- *developments relating to our 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 Annual Report on Form 10-K 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 Annual Report on Form 10-K 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 Annual Report on Form 10-K, 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 Annual Report on Form 10-K that modify or impact any of the forward-looking statements contained in this Annual Report on Form 10-K will be deemed to modify or supersede such statements in this Annual Report on Form 10-K.

PART I

Item 1. Business

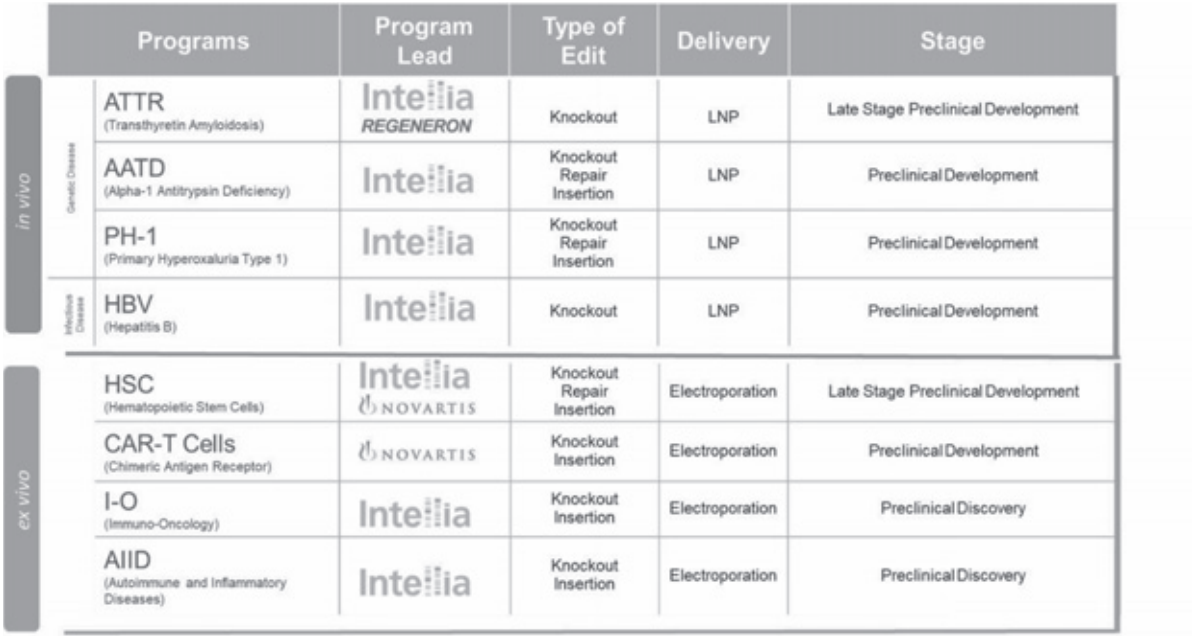
Overview

We are a leading genome editing 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 transform medicine 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 better target cancer and immunological diseases using engineered immune cells. 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 a potential new class of therapeutic products.

In 2012, one of our co-founders and current scientific advisors, Dr. Jennifer Doudna, and her colleagues published a paper in the journal *Science* describing the use of CRISPR/Cas9 as a genome editing tool. Genome editing is the precise and targeted modification of the genetic material of cells or viruses. Since the publication of Dr. Doudna's landmark paper, thousands of research papers have been published on the CRISPR/Cas9 technology. The CRISPR/Cas9 system offers a revolutionary approach for therapeutic development due to its broad potential to precisely edit the genome. This system can be used to make three general types of edits: knockouts, repairs and insertions. Each of these editing strategies takes advantage of naturally-occurring biological mechanisms to effect the desired genetic alteration. By addressing the underlying cause of the disease, this approach has the potential to provide curative therapeutic options for patients with genetically-based diseases.

We plan to use the CRISPR/Cas9 system across two broad areas: *in vivo* applications, in which CRISPR/Cas9 therapeutic products are delivered directly to target cells within the body; and *ex vivo* (outside the body) applications, in which human cells are modified or repaired using CRISPR/Cas9, and the edited cells are administered to the patient to replace the patient's abnormal cells, to target cancer cells or to regulate abnormal immune function. Our *in vivo* pipeline includes proprietary programs targeting genetic diseases including transthyretin amyloidosis (ATTR), which we are co-developing with Regeneron Pharmaceuticals, Inc. (Regeneron), alpha-1 antitrypsin deficiency (AATD) and inborn errors of metabolism (IEMs) such as primary hyperoxaluria (PH-1), and infectious diseases such as chronic hepatitis B infection (HBV). Our *ex vivo* pipeline consists of two separate efforts: 1) a set of proprietary programs within our internal eXtellia division focused on developing engineered cell therapies to treat various oncological and autoimmune diseases, and 2) partnered programs developed in collaboration with Novartis Institutes for BioMedical Research, Inc. (Novartis), focused on chimeric antigen receptor T cells (CAR-T cells) and hematopoietic stem cells (HSCs), the stem cells from which all of the various types of blood cells originate.

The following table illustrates our current discovery programs and opportunities as of February 28, 2018:



		Programs	Program Lead	Type of Edit	Delivery	Stage
in vivo	Genetic Disease	ATTR (Transthyretin Amyloidosis)	Intellia / REGENERON	Knockout	LNP	Late Stage Preclinical Development
		AATD (Alpha-1 Antitrypsin Deficiency)	Intellia	Knockout Repair Insertion	LNP	Preclinical Development
		PH-1 (Primary Hyperoxaluria Type 1)	Intellia	Knockout Repair Insertion	LNP	Preclinical Development
	Infectious Disease	HBV (Hepatitis B)	Intellia	Knockout	LNP	Preclinical Development
ex vivo		HSC (Hematopoietic Stem Cells)	Intellia / NOVARTIS	Knockout Repair Insertion	Electroporation	Late Stage Preclinical Development
		CAR-T Cells (Chimeric Antigen Receptor)	NOVARTIS	Knockout Insertion	Electroporation	Preclinical Development
		I-O (Immuno-Oncology)	Intellia	Knockout Insertion	Electroporation	Preclinical Discovery
		AIID (Autoimmune and Inflammatory Diseases)	Intellia	Knockout Insertion	Electroporation	Preclinical Discovery

In September 2017, we presented data from our completed long-term, 52-week, durability mouse study, demonstrating *in vivo* genome editing following a single, intravenous administration of CRISPR/Cas9. With a single dose, we achieved and maintained an approximately 97 percent reduction in serum TTR protein levels through 12 months. This TTR reduction was accomplished by approximately 70 percent sustained editing at the target DNA site in the liver. This study confirmed that our lipid nanoparticle (LNP) system is transiently present with 99 percent clearance of messenger RNA (mRNA) within 10 hours and of single guide RNA (sgRNA) within 72 hours in the liver. The treatment was well-tolerated at the time of administration and no adverse events were noted throughout the 52-weeks of follow up. These mouse durability results followed our presentation in August 2017 of initial data from rat studies demonstrating *in vivo* genome editing after a single, intravenous administration of CRISPR/Cas9. In our August 2017 presentation, we reported that, using our LNP system in rats, we had observed up to 91 percent reduction in serum TTR protein levels and up to 66 percent editing at the target DNA site in the subject animals.

In October 2017, we released interim top-line data regarding our *in vivo* non-human primate (NHP) exploratory pre-clinical studies. Specifically, based on preliminary studies currently at varying points of progress, liver genome editing rates using CRISPR/Cas9 delivered via our proprietary LNP system have ranged from 0.10 percent up to 32.0 percent after a single dose with various exploratory NHP guide RNAs (gRNA), LNP formulations and dosing regimens as well as with exploratory human cross-reactive gRNAs. In NHPs redosed with a subsequent application of our LNP formulations, we observed further editing that surpassed those levels achieved after a single dose, with multiple animals achieving a total of over 20 percent liver genome editing after a second dose.

These NHP results were similar to the results we observed in our initial rodent studies. We are conducting further improvements of our delivery system and proceeding to human guide selection. We expect to achieve higher levels of editing and reductions in serum levels of TTR protein that we achieved when we optimized the delivery system and CRISPR/Cas9 cargo used in our rodent models. We expect to begin Investigational New Drug (IND)-enabling activities for a human therapeutic as soon as mid-2018.

To date, in both single and repeat dose experiments, our proprietary LNP delivery system has been well-tolerated with both NHP-specific gRNA and exploratory human cross-reactive gRNAs, as assessed by gross observation of the animals, clinical chemistry, hematology, and cytokine and complement levels. We are also encouraged by the reduction in serum TTR protein levels shown to date in animals with the highest levels of editing. We are conducting additional studies in multiple animal models to maximize editing rates through repeat dosing and formulation improvements.

In October 2017, we presented data from an *in vivo* mouse study showing, after a single intracerebral injection, delivery to the brain of 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 gene 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, editing levels from less than 1% up to 28% were achieved in the striatal and cerebellar tissue. The injections were well tolerated and the mice did not display any behavioral changes post dosing.

In December 2017, our collaborator Novartis presented initial data from our research collaboration on genome-edited human hematopoietic stem cells. 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 stably engraft in mice while maintaining their desired properties. Specifically, the data showed that approximately 80-95 percent target site modification in human hematopoietic stem and progenitor CD34+ cells was achieved following electroporation of ribonucleoprotein (RNP) composed of Cas9 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 γ-globin transcript and 30-40 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 γ-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.

We believe our product focus, therapeutic discovery and development strength, delivery expertise and intellectual property 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 risk-mitigating approach with our initial indications and programs. Our approach is defined by four primary criteria: (i) the type of edit—knockout, repair or insertion; (ii) the delivery modality for *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 current *in vivo* programs focus on diseases attributable to genes expressed in the liver that have significant unmet medical needs – transthyretin amyloidosis, which we are co-developing with Regeneron, alpha-1 antitrypsin deficiency, primary hyperoxaluria and chronic hepatitis B infection – and our *ex vivo* programs are focused on applications of the technology in CAR-T cell and HSC, product candidates which are selectively partnered with our collaborator Novartis, and other engineered cell therapies to treat various oncological and autoimmune diseases that we are developing independently.

These selection criteria position us to build a diversified pipeline, in which we are not reliant on any single delivery technology or editing approach for success. In addition, we believe we can apply the learnings from these indications and programs to inform our selection of subsequent indications and targets of interest. We believe this approach serves to increase our probabilities of success in the indications for our current programs, generate insights that will accelerate the development of additional therapeutic products and broaden the opportunity for potential strategic alliances.

Delivery plays a key role in our *in vivo* therapeutic approach. We have shown in animal models that LNP delivery technology, which involves encapsulating therapeutic agents into microscopic lipid droplets, can systemically deliver CRISPR/Cas9 components to the liver, our initial organ of focus for *in vivo* applications. We have also successfully delivered CRISPR/Cas9 components to the brain in animal models using direct injection of LNPs. With our team's expertise with LNP delivery technology, we expect to translate the LNPs in our preclinical development to clinical development in humans. In parallel, we are exploring additional *in vivo* delivery vehicles, including viral delivery vectors, which are viruses engineered to carry non-viral nucleic acids to patients' cells, which we believe may assist us in treating genetic disease in other organs.

To explore the scope of gene edits with the CRISPR/Cas9 system, we have chosen four *in vivo* liver indications employing different editing strategies:

- ATTR program, which utilizes a gene knockout strategy;
- AATD program, which can utilize gene knockout, insertion or repair strategies;
- PH-1, our lead IEM program, which can utilize a gene knockout strategy or targeted DNA insertion; and
- HBV program, which utilizes a knockout strategy to target covalently closed circular DNA (cccDNA).

In addition to giving us four potential product opportunities, each of these programs will provide us with learnings that we intend to translate to a broader set of disease indications requiring the same types of edits in the liver and other organs.

Our partnered *ex vivo* programs in CAR-T cell and HSC applications are being developed with Novartis, where we retain the right to develop and commercialize rights to certain HSC programs. In CAR-T cell therapy, naturally-occurring immune cells, specifically T cells, are removed from a patient's body and modified *ex vivo* by inserting a chimeric antigen receptor (CAR) to selectively target cancer cells by activating an immune response against them. The CAR is an engineered fusion protein expressed on a cell's surface with an antibody-based portion that can recognize certain markers on other cells, such as cancer cells, and a signaling portion inside the cell that can deliver the desired signals when the antibody portion binds its markers. We believe CRISPR/Cas9 can further enhance CAR-T cells by, for example, generating a universal donor CAR-T cell or modifying genes that regulate T cell behavior to increase the therapeutic potential of a CAR-T cell therapy. In the HSC programs, we can apply CRISPR/Cas9 to correct defective proteins in HSCs of a given patient for the potential treatment of blood disorders or primary immune deficiencies. In additional applications, normal HSCs may be engineered *ex vivo* using CRISPR/Cas9 to produce cells expressing a therapeutic protein, and the cells are then returned to patients in need of that protein.

eXtellia is exploring the application of CRISPR/Cas9 gene editing in the fields of immuno-oncology beyond CAR-T cells, as well as applications of cell therapy in autoimmune and inflammatory diseases. Current focus is on developing products based on immune cells for which we retain proprietary rights, such as T cell receptor (TCR)-engineered T cells for immuno-oncology applications, engineered T regulatory cells (Tregs) for autoimmune disorders and other cell types such as engineered induced pluripotent stem cells. Our *ex vivo* delivery approach is a clinically proven delivery method called electroporation, an electrical charge-based technique for delivering molecules into cells, which has been used in advanced clinical studies. In parallel, we are considering other delivery methods for *ex vivo* introduction of biological material to cells, which may provide advantages in delivery efficiency or cell viability.

We believe our focused approach to selecting our initial and current *in vivo* and *ex vivo* programs positions us to build a pipeline across a range of indications and generate a wealth of data for opening up the potential therapeutic applications of the CRISPR/Cas9 technology across a broad range of diseases. Our collaboration and intellectual property strategies focus on leveraging existing third-party expertise in therapeutic research, preclinical and clinical development, regulatory affairs, manufacturing and commercialization, while also enhancing our industry-leading access to evolving genome editing technology, potential new therapeutic targets and delivery vehicles. Through our product research and development programs, we believe we can apply CRISPR/Cas9 technology to improve the lives of patients with significant unmet medical needs.

Strategy

Our goal is to build a fully integrated, product-driven biotechnology company, focused on developing and commercializing curative CRISPR/Cas9-based therapeutics. Our approach to advancing the broad potential of genome editing includes plans to:

Focus on Indications that Enable Us to Fully Develop the Potential of the CRISPR/Cas9 System. To maximize our opportunity to rapidly develop clinically successful products, we have applied a risk-mitigated approach to selecting indications with significant unmet medical needs based on four primary criteria:

- the type of edit: knockout, repair or insertion;
- the delivery modality for *in vivo* and *ex vivo* applications;
- the presence of established therapeutic endpoints; and
- the potential for the CRISPR/Cas9 system to provide therapeutic benefits when compared to existing therapeutic options.

We believe these selection criteria position us to build a diversified pipeline, in which we are not reliant on any single delivery technology or editing approach for success. In addition, we believe we can apply the learnings from our current programs to inform our selection of additional indications and targets of interest. We are also exploring ways to identify potential new therapeutic targets suitable for modulation with the CRISPR/Cas9 technology. We believe this approach serves to increase the probabilities of success in our initial indications, generate insights that will accelerate the development of additional therapeutic products and broaden the opportunity for potential strategic alliances.

Aggressively Pursue* In Vivo *Liver Indications to Develop Therapeutics Rapidly with Existing Delivery Technology. For our *in vivo* indications, we selected well-validated targets in diseases with significant unmet medical needs where there are predictive biomarkers, or measurable indicators of a biological condition or state, with strong disease correlation and where the CRISPR/Cas9 technology and delivery tools existing today could be applied towards developing a novel therapeutic. Our initial *in vivo* pipeline opportunities target diseases of the liver, which we believe we can develop using our existing LNP delivery technology. Among the first *in vivo* indications that we are evaluating are ATTR, AATD, PH-1, and HBV.

Actively Develop and Expand* Ex Vivo *Therapeutic Programs. Through eXtellia we are independently researching and developing proprietary engineered cell therapies to treat various oncological and autoimmune diseases, for example using TCR-engineered T cells for immuno-oncology applications, engineered Tregs for autoimmune disorders and other cell types such as engineered induced pluripotent stem cells. Further, in collaboration with Novartis, we are pursuing CAR-T cell and HSC programs. We believe that our work in CAR-T cells and HSCs help guide us in building our proprietary *ex vivo* portfolio.

Continue to Leverage Strategic Partnerships to Accelerate Clinical Development. We view strategic partnerships as important drivers for accelerating the achievement of our goal of rapidly developing curative therapies. The potential application of CRISPR/Cas9 is extremely broad, and we plan to continue to identify partners who can contribute meaningful resources and insights to our programs and allow us to more rapidly bring scientific innovation to a broader patient population. Our partnership focusing on CAR-T cells with Novartis, an industry leader with one of the most advanced clinical and commercial CAR-T cell programs, our partnership on *in vivo* liver indications with Regeneron, a leader in genetics-driven drug discovery and development, and our research collaboration initiated in 2017 on engineered T cell therapies with Ospedale San Raffaele, a leading European research-university hospital, exemplify this strategy.

Grow Our Leadership Position in the Field of Genome Editing. We are committed to broadening our capabilities to remain at the cutting edge of genome editing research. We will continue to invest internally in developing our platform capabilities, including innovative delivery modalities, technologies and tools to advance our therapeutic programs. We will also systematically explore accessing external technologies or opportunities to enhance our leadership position in developing innovative therapeutics.

Our Platform

An integral part of developing our therapeutic product candidates and exploring additional potential applications of CRISPR/Cas9 to future indications includes building and improving on various proprietary and in-licensed aspects of our technology platform. We continue to develop robust, high volume (high-throughput) capabilities centering around CRISPR/Cas9 components, editing strategies and delivery methods that we believe will provide us with a competitive advantage in creating successful therapeutic product candidates.

Informatics

We have built a high-throughput, scalable data processing and analysis, or informatics, infrastructure to support various aspects of our platform, including guide ribonucleic acid (RNA) selection and analysis of on- and off-target editing in cells. Depending on the desired editing strategy, we use our proprietary bioinformatics methods to design candidate guides and select those that we believe are more likely to be highly specific and have high cutting efficiency. As we grow our experimental data set, we continue to incorporate guide performance into our algorithms to improve their predictive power.

Guide RNA Qualification

As part of the process to identify guide RNAs for potential development candidates, we screen numerous guide RNAs for their ability to generate the required edit at the genomic site of interest, called on-target activity, as well as any propensity to generate unwanted events at other sites in the genome, also known as off-target activity. To evaluate on-target activity, we use high-throughput sequencing methods to analyze the genomes of edited cells, allowing us to assess overall editing efficiency and to examine the nature of the editing events, such as specific insertions or deletions.

For guide RNAs selected through our primary on-target screens, we perform a variety of analyses to look for possible off-target editing events, including bioinformatic predictions and experimental methods. Part of our approach involves identifying candidates with no or few off-target sites based on experimental measurements of genome-wide DNA breaks, as well as targeted sequencing of such candidate sites to evaluate actual off-target editing events in relevant cell types. We continue to optimize our guide RNA qualification capability over time by increasing our throughput, improving our off-target activity detection accuracy and increasing our bioinformatics predictive accuracy.

Guide RNA format

CRISPR/Cas9 systems can function with guide RNAs having a variety of modifications, such as changes to the physical guide RNA structure or chemical modifications of nucleotides. As part of our development of CRISPR/Cas9 therapeutics, we are engineering modified guide RNAs to, for example, improve editing efficiency and targeting, as well as to reduce the likelihood of an immune response. We believe our work in this area will allow us to develop the most appropriate guides for therapeutic applications.

Nuclease

Our current preferred Cas9 protein is derived from a type of bacteria called *S. pyogenes* (*Spy*), which is the Cas9 used in the vast majority of published CRISPR/Cas9 literature to date. As part of the therapeutic development process, we are adapting and engineering *Spy* Cas9 with the goal of improving its specificity, activity and manufacturability. In addition, we are exploring other naturally-occurring Cas9 proteins and nucleases from other organisms, which may differ from *Spy* Cas9 in aspects such as specificity, size or mechanism of DNA cut. We are pursuing these alternative Cas9 forms and other nucleases through ongoing internal work, by collaborating with our existing partners and scientific founders and by investigating in-licensing opportunities. We are also investigating targeted modifications of Cas9 that can modulate DNA activity by mechanisms other than cleavage. We believe that different therapeutic applications may be best addressed using different forms of Cas9 or other nucleases, depending on the target cell or tissue of interest, the delivery method and the desired type of edit.

Cas9 Edit type

While knockout edits can be made using solely a Cas9 protein and guide RNA, repair and insertion edits additionally require a template nucleic acid that contains the desired corrected or inserted sequence. The way in which the template is provided depends on the delivery modality. For example, for *ex vivo* applications, the DNA template may be delivered by electroporation in combination with a Cas9-guide RNA complex. We are also investigating various *in vivo* strategies for delivering repair and insertion templates, such as delivery by LNPs or by viral vectors. Further, we are developing methods to selectively promote template-based repair or insertion mechanisms in cells, as opposed to non-template-based repair that otherwise may generate knockout edits.

In vivo *delivery*

We are focusing our initial *in vivo* applications in the liver, with delivery of CRISPR/Cas9 components by LNPs.

LNPs encapsulate the therapeutic material, providing it with stability, targeted delivery capabilities, improved pharmacologic properties and controlled circulation time, allowing for transient expression of Cas9. We see multiple advantages of using LNPs as our initial *in vivo* delivery vehicle, particularly as optimized by us for delivery of the CRISPR/Cas9 system or its components. Certain LNPs have demonstrated efficacy, safety and favorable tolerability and are currently used as a delivery system for therapeutic small interfering RNA (siRNA) as well as therapeutic mRNA. mRNA is RNA that encodes proteins, while siRNA is RNA that can interfere with the function of mRNA. There are currently several LNP/siRNA programs of other companies in the clinic, with the most advanced having successfully completed Phase III development, leading to a New Drug Application (NDA) filing. LNP delivery of CRISPR/Cas9-based therapies, where potentially only one or few treatment courses are needed, has the potential to show a more favorable safety profile when compared to therapeutic modalities like siRNAs where chronic dosing is needed. Additionally, LNPs are chemically well-defined and have a completely synthetic route of manufacture, which permits greater scalability. We are currently advancing our programs using a set of biodegradable, well-tolerated lipids, which are based on lipids originally developed by Novartis and in-licensed for use with CRISPR/Cas9 products. To date, we have successfully demonstrated *in vivo* editing in various animal models, including in mouse, rat and non-human primate livers, with a single dose of systemically delivered LNPs based on these lipids. We have also shown successful delivery and editing in mouse brain using CRISPR/Cas9 delivered by direct injection of one of our proprietary LNP formulations. The injections were well tolerated and the mice did not display any behavioral changes.

With our team's expertise in LNP delivery technology, we expect to be able to translate the LNPs that we are using for our preclinical evaluation to clinical development in humans. In addition, we are exploring options for incorporating Cas9 into therapeutic products in multiple formats. For example, Cas9 can be delivered in its protein form or could be delivered as a nucleic acid, such as an mRNA. For delivery of Cas9 mRNA, we are also investigating modifications that may improve expression and stability, as well as reduce the potential for an immune response. We plan to continue to further improve on LNP formats for a variety of CRISPR/Cas9 therapeutic components, including templates for repair and insertion edits. In parallel, we are exploring additional delivery vehicles, including synthetic particles and viral vectors, that we believe will allow us to target the central nervous system, eye, muscle and other organs.

Ex vivo *delivery*

Cellular therapies are based on the administration of engineered human cells that are modified to provide or restore necessary functions in the cells of patients, or to target and eliminate cells with harmful attributes, such as cancer cells. The cells to be modified *ex vivo* can come from the individual patient (autologous source) or from another individual (allogeneic source), and the modification takes place *ex vivo*. We use the CRISPR/Cas9 system to perform the modification, and deliver the system using a clinically proven method called electroporation, an electrical charge-based technique for delivering molecules into cells. In parallel, we are exploring other delivery methods for *ex vivo* introduction of biological material to cells, which may provide advantages such as delivery efficiency. In human cells, we have been able to achieve relatively high editing rates, including rates greater than 90%, of both copies of a single gene (bi-allelic editing), while preserving cell viability.

We have also simultaneously targeted multiple genes in an *ex vivo* setting and achieved high bi-allelic editing rates for both genes, demonstrating what we believe to be therapeutically relevant editing of multiple genes simultaneously (multiplex editing). The ability to achieve multiplex editing may be critical in targeting certain diseases.

Our Pipeline

To accelerate the development and commercialization of CRISPR/Cas9-based products in multiple therapeutic areas, we are targeting various indications using *in vivo* and *ex vivo* approaches to demonstrate proof-of-concept of the various facets of our technology, including the type of edit and CRISPR/Cas9 selectivity and efficiency. We believe that the learnings we gain from each indication will pave the way for rapid expansion of our pipeline by allowing us to target subsequent indications that use the same or analogous delivery vehicles, guide structures and types of edits.

We believe that effective delivery methods will be important for the clinical success of the CRISPR/Cas9 system. Our approach is to undertake a parallel effort on both *in vivo* and *ex vivo* delivery that leverages nearly two decades of research and development in nucleic acid therapeutics and capitalizes on currently available, clinically and preclinically validated technologies, while developing next-generation delivery methods optimized for the CRISPR/Cas9 system.

In Vivo *Pipeline*

Our initial *in vivo* indications target genetic liver diseases, including ATTR, AATD and PH-1, and infectious diseases such as HBV. Our initial efforts on *in vivo* delivery focus on the use of LNPs for delivery of the CRISPR/Cas9 complex to the liver.

Genetic diseases:

Transthyretin Amyloidosis Program (Knockout Strategy)

Transthyretin (TTR) is a protein produced primarily in the liver, encoded by the *TTR* gene. This protein carries retinol (vitamin A) and thyroxine (thyroid hormone) throughout the body. Certain mutations can cause the protein to aggregate and accumulate in tissues, resulting in a disorder called TTR-mediated amyloidosis (ATTR). Over 120 different genetic mutations are currently known to cause ATTR. Protein accumulation in peripheral nerves or the heart can result in a severe loss of nerve or cardiac function. Mutations leading to nerve disease cause a syndrome called familial amyloidotic polyneuropathy (FAP), whereas those leading to heart disease cause a syndrome called familial amyloidotic cardiomyopathy (FAC). Ongoing amyloid deposition in tissues due to disease progression results in the development of cardiomyopathy and other cardiac symptoms observed in FAC patients. Typical onset of disease symptoms occurs during adulthood and can be fatal within two to 15 years. Estimates suggest that approximately 50,000 patients suffer from ATTR worldwide.

We believe that we can apply CRISPR/Cas9 technology to potentially cure ATTR by knocking out expression of the *TTR* gene in the liver. We expect this approach to greatly reduce or eliminate the production of the TTR protein, which should slow or stop the accumulation of protein in the nerves and the heart. Current treatments and ongoing clinical trials in FAP have shown a significant correlation between TTR protein reduction and clinical benefit. Additionally, these studies suggest that loss of *TTR* gene expression from the liver would be well-tolerated in adult humans. Accordingly, we believe targeting *TTR* genes with CRISPR/Cas9 may improve patient outcomes by potentially eliminating defective TTR protein in a single or small number of treatments, as opposed to life-long therapy. We have assessed delivery of guide RNAs directed at the *TTR* gene via LNPs and have achieved high levels of liver cell editing *in vitro* and *in vivo* as well as reduction of serum TTR protein in multiple species. In mice, with a single dose of LNP, we achieved and maintained an approximately 97 percent reduction in serum TTR protein levels through 12 months. This TTR reduction was accomplished by approximately 70 percent sustained editing at the target DNA site in the liver. In rats, we have observed up to 91 percent reduction in serum TTR protein levels and up to 66 percent editing at the target DNA site in the subject animals.

In preliminary NHP studies currently at varying points of progress, we achieved liver genome editing rates using CRISPR/Cas9 delivered via our proprietary LNP system ranging from 0.10 percent up to 32.0 percent after a single

dose with various exploratory gRNA, LNP formulations and dosing regimens. In NHPs redosed with a subsequent application of our LNP formulations, which were well tolerated, we observed further editing surpassing the levels achieved after a single dose. We continue to improve upon our current LNP formulations, and expect to begin IND-enabling activities for a human therapeutic as soon as mid-2018.

Clinical Development Pathway

Our first in-human studies in ATTR are expected to take place in patients with ATTR who have started to exhibit symptoms related to amyloid deposition. The key objective of these studies will be to show that the therapy can be delivered safely to the patient. A secondary objective will be to identify early indicators of efficacy, which may include reductions in serum levels of TTR protein. We expect that the results of our preclinical studies, and discussions with the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA) and other relevant regulatory agencies as well as patient advocacy groups will be important in informing our trial design. Under our collaboration agreement, we expect to co-develop therapies targeting ATTR with Regeneron.

Alpha-1 Antitrypsin Deficiency Program (Knockout, Repair, and Insertion Strategies)

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

The most common form of AATD arises when a patient has a mutation in both copies of the *SERPINA1* gene, which causes AAT to aggregate inside liver hepatocytes, rather than being secreted from the liver. The inability to secrete AAT leaves the lung unprotected from neutrophil elastase and can result in pulmonary disease. The pulmonary consequences of AATD can sometimes culminate in COPD. Estimates suggest that between 1% and 2% of all cases of COPD in the United States have AATD as the underlying cause. In some forms of the disease, AAT accumulates in the liver, causing liver inflammation and cirrhosis, which leads to liver damage, scarring and in the most severe cases, liver failure or cancer. Liver disease associated with AATD is diagnosed from infancy to adulthood, whereas lung disease is most common in adult patients.

We believe that we can apply the CRISPR/Cas9 technology to cure AATD by addressing the defective *SERPINA1* gene. We are evaluating multiple editing approaches—knockout, insertion and repair. Our knockout program for AATD will be best suited for patients with AATD-associated liver disease, as there is currently no effective way to reduce the accumulation of mutated AAT in the liver. With this strategy, we intend to eliminate production of the aberrant form of AAT by knocking out the mutated *SERPINA1* gene with a Cas9-mediated cut. We believe this knockout will halt the production and accumulation of AAT in the liver but will not by itself address the lack of AAT circulation that leads to lung disease. Therefore, in this approach, we expect that patients with AATD-associated lung disease may have to be treated with other therapies, such as plasma protein supplementation, to achieve levels of the normal form of AAT to be active against the lung disease.

We believe our insertion and repair approaches for AATD will address the lung disease as well as the liver disease. With either of these strategies, we intend to either insert a normal copy of the SERPINA1 gene or correct the mutated *SERPINA1* gene, which we believe will eliminate production of the aberrant form of AAT and also establish production of the normal protein in the liver. We believe both approaches could reduce or eliminate liver inflammation and increase levels of normal circulating AAT, which should protect the lung from neutrophil elastase, thereby reducing or eliminating the need for other therapies, such as plasma protein augmentation therapy. There is preclinical evidence that hepatocytes with normal AAT may possess a growth advantage over those that express the mutated form, suggesting that correction of only a limited number of hepatocytes might be sufficient to address this disease. We expect the progress of these strategies to follow our AATD knockout program. Depending on the results of our studies and potential development requirements and timelines, we may decide to pursue one or more of these programs in clinical development.

Clinical Development Pathway

Our first-in-human studies are expected to take place in patients with AATD. The key objective of these studies will be to show that the therapy can be delivered safely to the patient. A secondary objective will be to identify early indicators of efficacy, which may include reductions in levels of mutated AAT protein, increases in production of normal circulating AAT protein and the required tests for determining liver and lung function. We will also seek to observe whether we have achieved pre-determined levels of properly functioning AAT in the blood, which has been used historically as a biomarker for approval of augmentation therapy approaches. We expect that the results of our preclinical studies and discussions with the FDA, EMA and other relevant regulatory agencies as well as the AATD community will be important for selecting the appropriate patients and endpoints for our clinical trials.

Inborn Errors of Metabolism (IEM) Program (Knockout, Repair and Insertion Strategies)

IEMs span a range of conditions, many severe or fatal, and frequently untreatable. Current treatment options for many IEMs are unsatisfactory and often include bone marrow or liver transplants, which pose the challenge of serious side effects including high risk of mortality in some cases. Individual IEMs are rare disorders, many having an incidence of fewer than 1 in 100,000 births. These diseases typically involve defects in single genes that code for enzymes that facilitate the metabolism of certain cellular components. Mutations in these enzymes can result in accumulation of metabolic intermediates, which are molecules that are precursor compounds in the chemical pathway leading to final metabolic products, that are toxic or interfere with normal biology. We have selected our lead IEM program, primary hyperoxaluria type 1 (PH-1), and are evaluating a large set of additional candidate IEMs, including argininosuccinic lyase deficiency; ornithine transcarbamylase deficiency; phenylketonuria (PKU) and maple syrup urine disease. Our selection criteria for our additional IEM indications include identifying diseases that originate in the liver, have well-defined mutations that can be addressed by a single knockout, repair or insertion approach, have readily measurable therapeutic endpoints with observable clinical responses, and for which there are no effective treatments.

Infectious Diseases

Hepatitis B Virus Program (Knockout Strategy)

Hepatitis B is an infection of the liver caused by HBV that can progress from acute to chronic infection in approximately 5-10% of infected adults. Chronic HBV can result in long-term health problems, including liver damage, liver failure, liver cancer or even death. Chronic HBV affects approximately 240 million people globally and contributes to an estimated 786,000 deaths each year. In the United States, an estimated 700,000 to 1.4 million persons have chronic HBV, with 2,000 to 4,000 HBV-related deaths per year.

We believe that treatment of HBV with a CRISPR/Cas9-based therapeutic has the potential to cure the disease as it could eradicate cccDNA reservoirs with one or a few treatment courses, potentially as a single agent or in combination with other therapies. For this therapeutic program, we intend to use a knockout strategy to destroy or render inactive the copies of HBV cccDNA in infected human cells. We believe this therapy could offer a significant improvement over existing treatment options that are life-long and do not cure the disease. We also believe it is possible that a common treatment solution can be developed for many or all genotypes of HBV through targeting portions of the cccDNA sequences that are the same across genotypes. In addition, there is potential to reduce viral resistance as the virus itself is eradicated.

According to published research studies, CRISPR/Cas9-mediated cuts can significantly reduce intracellular levels of cccDNA when tested *in vitro*. We believe we can use the CRISPR/Cas9 system to help eliminate the reservoirs of cccDNA in infected HBV patients. We are evaluating different knockout approaches to eliminate cccDNA *in vivo*, including cleaving the cccDNA in various individual or a combination of locations.

We have screened all of the potential guides from a specific HBV genomic sequence for their ability to cut HBV DNA, and also completed a bioinformatic analysis of potential CRISPR/Cas9 target sites in the HBV genome to identify guides that can be effective across HBV genotypes. In addition, we have conducted *in vitro* studies to assess the cccDNA reduction activity of these transiently delivered guides, as well as their ability to reduce viral antigen production. We continue to explore animal systems to assess the ability of our guide RNAs to reduce the levels of HBV virus and antigens in an *in vivo* setting.

Clinical Development Pathway

We expect our clinical development path to indicate evidence of safety and antiviral activity in patients infected with HBV, as a single agent or in combination with other therapies. The key study objective will be to show that the therapy can be delivered safely to the patient, with a secondary objective of identifying early indicators of antiviral effect. We expect that the results of our preclinical studies and discussions with the FDA, EMA and other relevant regulatory agencies, as well as with the HBV community, will be important for selecting the appropriate patients and endpoints for any future clinical trial.

Ex Vivo *Pipeline*

Through eXtellia, we are independently researching and developing proprietary engineered cell therapies to treat *ex vivo* various oncological and autoimmune diseases, for example using TCR-engineered T cells for immuno-oncology applications, engineered Tregs for autoimmune disorders and other cell types such as engineered induced pluripotent stem cells. Our approach to these products includes multiple avenues. In particular:

- We seek to develop allogeneic cellular therapies, which are cells derived from unmatched donors and modified outside of the human body to allow them to be administered to an unrelated patient. This effort is supported through our relationship with certain researchers at the Karolinska Institutet.
- Outside our Novartis collaboration, we are exploring non-CAR-T cellular approaches that utilize immune cells, including TCR based therapy, to target immuno-oncology indications. For example, in our existing collaboration with Ospedale San Raffaele, we are identifying optimized TCR sequences of an antigen target that could be used to treat certain cancers.
- We are also exploring methods to apply CRISPR/Cas9 editing to CD4 cells to induce non-reverting regulatory T cell phenotype for therapies that address auto-immune disease.

Our partnered *ex vivo* programs are in CAR-T cell and HSC applications. Under our strategic collaboration with Novartis, our CAR-T cell program is exclusive to Novartis. We retain the right to develop and commercialize certain of the HSC programs that we discover with Novartis while others will be proprietary to Novartis.

For our *ex vivo* programs requiring delivery to extracted cells such as HSCs or T cells for modification, we initially plan to deliver the CRISPR/Cas9 complex by electroporation. In parallel with electroporation, we are exploring alternative technologies for delivery to cells *ex vivo* that may provide advantages in delivery efficiency or cell viability.

CAR-T Cell Program

In 2017, the first CAR-T cell products, including Novartis' *Kymriah* (CTL019), were approved by the FDA to treat certain oncology indications such as pediatric acute lymphoblastic leukemia (ALL) and Non-Hodgkins Lymphoma (NHL). Additional therapies are being developed for blood cancers such as acute myeloid leukemia (AML), multiple myeloma (MML) and chronic lymphocytic leukemia (CLL), as well as several other solid-rumor cancers. In CAR-T cell therapy, naturally-occurring immune cells, specifically T cells, are modified *ex vivo* by inserting a chimeric antigen receptor (CAR) into the T cells, thereby activating an immune response against cancer cells.

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

- CRISPR/Cas9 could be used to create a universal donor CAR-T cell by knocking out cell surface markers that cause a patient's immune system to recognize another person's cells as foreign. Allowing multiple patients to be treated using cells from a single donor could significantly streamline manufacturing and make CAR-T cell therapy more widely accessible.
- CRISPR/Cas9 could be used to modify the T cells to enhance their survival or activity against cancer cells.

- CRISPR/Cas9 could be used to introduce the CAR into a precise location in the genome with a specific integrated copy number, as opposed to the current method involving semi-random integration, thus potentially improving the safety profile of the resulting cells.
- CRISPR/Cas9 could be used to knockout one or more of the proteins believed to be responsible for certain serious side effects that can result in dangerously high fevers or severe loss of blood pressure.

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

HSC Program

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

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

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

CAR-T Cell and HSC Development Collaboration with Novartis

Under this collaboration, we received an upfront technology access payment from Novartis of $10.0 million and are entitled to up to an additional $40.0 million, in the aggregate, in additional technology access fees and research payments during the five-year collaboration term, subject to certain credits and adjustments in favor of Novartis. In addition, we are eligible to earn up to $230.3 million in development, regulatory and sales-based milestone payments and mid-single-digit royalties, in each case, on a per-product basis for the products developed by Novartis, subject to certain target-based limitations. For more information regarding our ongoing collaboration with Novartis, see the section below entitled "Collaborations—Novartis Institutes for BioMedical Research, Inc."

Collaborations

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

Novartis Institutes for BioMedical Research, Inc.

In December 2014, we entered into a strategic collaboration agreement with Novartis, primarily focused on the development of new *ex vivo* CRISPR/Cas9-based therapies using CAR-T cells and HSCs.

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, 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 investigational new drug 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 United States, (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.

We granted to Novartis a license to our CRISPR/Cas9 platform technology and Novartis granted us a non-exclusive license to its small molecule for HSC expansion and to its LNP platform technology to research, develop and commercialize HSC and *in vivo* products, respectively. Our license grant to Novartis of our CRISPR/Cas9 platform technology, including a sublicense to certain platform rights licensed from Caribou Biosciences, Inc. ("Caribou"), is exclusive in the HSC, CAR-T cell and *in vivo* fields with respect to each target selected by Novartis pursuant to the agreement and the research plan as long as Novartis continues to use commercially reasonable efforts to research, develop, and commercialize products directed to such targets. Upon the expiration of the collaboration term, Novartis shall have the option to access and obtain a non-exclusive license to our CRISPR/Cas9 platform technology to research, develop and commercialize potential therapeutic, prophylactic and palliative products and services for a limited number of certain approved targets selected by Novartis, exercisable upon written notice to us

within a specified time after the expiration of the collaboration term. Such approved targets are subject to certain restrictions, including that the targets may not have been already reserved by us pursuant to our limited right to do so under the agreement, may not be the subject of an existing out license of our CRISPR/Cas9 platform to a third party and may not be the subject of ongoing or planned research and development by us. This non-exclusive license will have a term of five years commencing upon the completion of the technology transfer by us enabling Novartis to practice such licensed rights, and Novartis may not select more than a specified number of approved targets in each year of this license term.

Intellectual property that we develop within the collaboration related to our CRISPR/Cas9 platform will be owned solely by us, while all other intellectual property developed within the collaboration, including intellectual property covering products arising from the collaboration, will be jointly owned by us and Novartis.

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

Regeneron Pharmaceuticals, Inc.

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 gene editing in the liver as well as a technology collaboration component, pursuant to which we and Regeneron will engage in research and development activities aimed at discovering and developing novel technologies and improvements to CRISPR/Cas technology to enhance our gene editing platform. Under this agreement, we also may access the Regeneron Genetics Center and proprietary mouse models to be provided by Regeneron for a limited number of our liver programs.

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 will be subject to a co-development and co-commercialization arrangement between us and Regeneron. We retain the exclusive right to solely develop products for certain indications, including AATD and HBV. 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 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 up to mid-single-digit royalty obligations under a license agreement with Caribou. In addition, Regeneron is obligated to fund 50.0% of certain research and development costs for the ATTR program, the first target selected by Regeneron, which will be subject to a co-development and co-commercialization arrangement between us and Regeneron.

We have granted Regeneron exclusive rights to develop and commercialize products directed to its selected targets. The parties will jointly own intellectual property created as part of the technology collaboration and target-specific research plans, subject to certain exceptions where Regeneron will solely own certain intellectual property specific to its products and we will solely own certain CRISPR/Cas intellectual property arising during target evaluation activities. Each party has granted the other party specified intellectual property licenses to enable the other party to perform its obligations and exercise its rights under the agreement, including license grants to enable each party to conduct research, development and commercialization activities pursuant to the terms of the agreement.

The collaboration term ends in April 2022, provided 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. We may terminate the agreement on a target-by-target basis if Regeneron or any of its affiliates institutes a patent challenge against our CRISPR/Cas or certain other background patent rights. We 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 us, 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 us, as described in the agreement. Following such termination, we will owe Regeneron royalties in the low to mid-single digits on any terminated targets that we subsequently commercialize 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.

Potential Future Collaborations

We view strategic partnerships as important drivers for helping accelerate our goal of rapidly treating patients. The potential application of CRISPR/Cas9 is extremely broad, and we plan to continue to identify partners who can contribute meaningful resources and insights to our programs and allow us to more rapidly bring scientific innovation to a broader patient population.

Intellectual Property

We believe we are well positioned in terms of our intellectual property because we:

- have built, and intend to expand, a broad worldwide portfolio of intellectual property, including patents and patent applications, in areas relevant to the development and commercialization of human therapeutic products using CRISPR/Cas9 technology;
- protect our intellectual property by maintaining trade secrets relating to our proprietary technology innovations and know-how; and
- intend to take additional steps, where appropriate, to further protect our intellectual property rights, including, for example, through the use of copyright protection and regulatory protection available via orphan drug designations, data exclusivity, market exclusivity, and patent term extensions.

Our licensed patent portfolio encompasses foundational filings on the use of CRISPR/Cas9 systems for gene editing, improvement modifications of these CRISPR systems, LNP technologies for delivering protein/nucleic acid complexes and RNA into cells, and cell expansion technology relevant to stem cell-based therapies. We access these patent estates through licenses from Caribou and Novartis. We also actively apply for, maintain, and plan to defend and enforce, as needed, our internally developed and externally licensed patent rights. Furthermore, we continue to search for and evaluate opportunities to in-license intellectual property relevant to our targeted therapeutic programs and platforms and to develop and acquire new intellectual property in collaboration with third parties.

Our portfolio of patent rights includes the following:

Caribou Biosciences In-Licensed Intellectual Property

In July 2014, we entered into a license agreement with Caribou, as subsequently amended and supplemented, for an exclusive, worldwide license for human therapeutic, prophylactic, and palliative uses, except for anti-fungal and anti-microbial uses, defined in the license agreement as our field of use, of any CRISPR/Cas9-related patents and applications owned, controlled or licensed by Caribou as well as companion diagnostics to our product or product candidates. The license agreement also included exclusive rights in our field of use to any CRISPR/Cas9-related intellectual property developed by Caribou after July 16, 2014 and through a cut-off date of January 30, 2018. The agreement further includes a non-exclusive research license to conduct research and development on product candidates and products. The Caribou licensed patent portfolio includes several U.S. and foreign patents and patent applications owned by Caribou, and U.S. and foreign patents and patent applications co-owned by The Regents of the University of California, the University of Vienna and Dr. Emmanuelle Charpentier, as well as U.S. and foreign patents and patent applications owned or controlled by Pioneer Hi-Bred and its affiliates. We have the right to grant sublicenses to the Caribou licensed patent portfolio to third parties in our field of use. Caribou retains the right to practice the licensed intellectual property in all other fields, including for its own specific therapeutics purposes, provided it does not pertain to the application of CRISPR/Cas9 technology to the development of products in our field of use.

Pursuant to a services agreement entered into with Caribou in parallel with the license agreement, we also received two years of research and development services from Caribou, which ended in November 2016. Any intellectual property developed under the services agreement is owned by Caribou and is included in, and subject to the terms of, our license agreement with Caribou.

In relation to our founding, we issued Caribou 8,110,599 shares of our junior preferred stock. We paid Caribou $5.0 million over the term of the two-year services agreement; and have agreed to pay 30.0% of Caribou's patent prosecution, filing, and maintenance costs for the intellectual property included in the license agreement amounting to a total of $2.6 million paid through December 31, 2017. We also granted Caribou an exclusive, royalty-free, worldwide license, with the right to sublicense, to any CRISPR/Cas9 patents, patent applications and know-how in Caribou's retained fields of use owned or developed by us between July 16, 2014 and a cut-off date of January 30, 2018. Caribou, which is obligated to pay a portion of our patent filing, prosecution and maintenance costs for any such licensed intellectual property, also has an option to sublicense any CRISPR/Cas9 intellectual property in-licensed by us for uses and activities in its retained field of use.

The Caribou license agreement grants us sublicenses in our field of use to intellectual property in-licensed by Caribou from The Regents of the University of California and the University of Vienna. Further, under the license agreement, we had an option to sublicense for our field of use any new intellectual property in-licensed by Caribou through January 30, 2018. In July 2015, we exercised our option to sublicense a portfolio in-licensed by Caribou from Pioneer Hi-Bred International, according to the terms described below.

The term of the Caribou license is until the expiration of the last-to-expire patent right that is licensed to either party. We must use commercially reasonable and diligent efforts to research, develop, manufacture and commercialize at least one product. Either party may terminate the agreement in the event of the other party's uncured material breach, bankruptcy or insolvency-related events, or breach of its obligations with respect to the included in-licenses. The license agreement with Caribou also gives us access, in our field of use, to Caribou internally developed IP. Since March 2013, Caribou has filed over 50 patent applications in the United States and internationally, which relate to the CRISPR/Cas platform, including modified and improved CRISPR/Cas9 systems or components, and methods of use that are part of our license. We cannot ensure that these applications will lead to issued claims that cover our products or activities. Any patents that grant from these applications will expire in or after 2034, assuming payment of necessary maintenance fees.

The Regents of the University of California and the University of Vienna Intellectual Property

The Regents of the University of California and the University of Vienna (collectively, UC/Vienna) co-own with Dr. Emmanuelle Charpentier a worldwide patent portfolio, which covers methods of use and compositions relating to engineered CRISPR/Cas9 systems for, among other things, cleaving or editing DNA and altering gene product expression in various organisms, including humans. We refer to this co-owned worldwide patent portfolio as the UC/Vienna/Charpentier patent family. The earliest claimed priority date for this patent family is May 25, 2012. As of December 31, 2017, this family includes granted patents in many jurisdictions outside the United States, including for example the United Kingdom, Germany, Australia, China and the approximately 40 countries that are members of the European Patent Convention. Corresponding applications are being prosecuted in the United States Patent and Trademark Office (USPTO) and other patent agencies across the world. Any patents that ultimately issue from this family and are appropriately maintained will expire in or after 2033.

Caribou entered into an exclusive, worldwide license in all fields, with the right to sublicense, for this patent family with UC/Vienna in April 2013 solely under UC/Vienna ownership rights. Caribou's license remains in effect for the life of the last-to-expire patent or last-to-be-abandoned patent application licensed, whichever is later. Through our license agreement with Caribou, we have an exclusive sublicense to UC/Vienna's interest in this foundational CRISPR/Cas9 patent family for use in human therapeutics, except for anti-fungal and anti-microbial uses as defined in the license agreement as our field of use. For products covered by this license and their companion diagnostics, we will owe mid-single-digit royalties on net sales. In addition, we may be subject to milestone payments of $0.1 million upon the first filing of an investigational new drug application, a total of $0.5 million for Phase II and Phase III clinical trials, $0.5 million to $1.0 million for each of the first three approved new drug applications or biologics license applications in the United States, and $0.2 million for each of the first three approved indications in Europe. Caribou has the right to terminate its agreement with UC/Vienna at any time or the agreement may be terminated due to an uncured material breach. We cannot guarantee that Caribou will maintain the UC/Vienna license for its full term. Should the license between Caribou and UC/Vienna be terminated for any reason, any compliant Caribou sublicenses as of the termination date will remain in effect and will be assigned to UC/Vienna in place of Caribou. Specifically, if we are in compliance with our obligations under our sublicense and Caribou and UC/Vienna terminate their agreement, UC/Vienna would replace Caribou as our licensor.

On April 13, 2015, UC/Vienna and Dr. Charpentier (collectively, UC/Vienna/Charpentier) jointly filed a request with 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 and the President and Fellows of Harvard College (collectively, the Broad Institute patent family), which claim aspects of CRISPR/Cas9 systems and methods to edit genes in eukaryotic cells, including human cells. The Broad Institute patent family includes, for example, US 8,697,359, issued on April 15, 2014. The earliest claimed priority date for the Broad Institute patent family is December 12, 2012. On January 11, 2016, the Patent Trial and Appeal Board (PTAB) of the USPTO declared an interference involving one UC/Vienna/Charpentier application, 12 Broad issued patents and a Broad patent application. On February 15, 2017, the PTAB dismissed the proceeding finding that the respective patent claims involved in the interference were distinct such that they did not meet the legal requirement to proceed with

the interference. 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 to terminate the interference, and briefing on the appeal was completed in November 2017. Unless otherwise resolved, the Federal Circuit is expected to render a decision after an oral hearing. In addition, UC/Vienna/Charpentier continue to prosecute other patent claims covering the CRISPR/Cas9 inventions, which could also result in allowable or issued patents in the United States. Certain of the claims being prosecuted by UC/Vienna/Charpentier, if found allowable by the USPTO, could lead to interference proceedings against patents or patent applications owned by other parties, including the Broad Institute patent family with respect to certain claims relating to the use of CRISPR/Cas9 in eukaryotic cells. We cannot be certain which of these results, if any, will actually occur or at what time, and the effects that any such results may have on us and our intellectual property position are currently unknown.

Pioneer Hi-Bred International (DuPont Company) Intellectual Property

Pioneer Hi-Bred and its affiliates, including the DuPont Company, have licensed to Caribou on a worldwide basis, various patent families relating to CRISPR/Cas systems, components and methods of use generally and CRISPR/Cas9 specifically in certain fields, which include Intellia's field of use under our license agreement with Caribou. In July 2015, we exercised our option under the license agreement with Caribou to sublicense these Pioneer patent families in our field of use. The license from Pioneer to Caribou will expire upon the expiration, abandonment or invalidation of the last patent or patent application licensed from Pioneer to Caribou.

The licensed Pioneer portfolio includes a family of applications filed by Vilnius University that discloses the components of a CRISPR/Cas9 system required for gene editing in non-bacterial organisms. On May 2, 2017, the USPTO issued U.S. Patent No. 9,637,739, with claims covering the *in vitro* assembly and use of a recombinant CRISPR/Cas9 complex to modify DNA. Patents obtained from this patent family will expire in or after 2033, assuming payment of necessary maintenance fees. We cannot ensure that these additional applications in this family will lead to issued claims that cover our products or activities.

Invention Management Agreement

On December 15, 2016, we entered into a Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement (the Invention Management Agreement), with The Regents of the University of California, University of Vienna, Dr. Charpentier, Caribou, CRISPR Therapeutics AG, ERS Genomics Ltd. and TRACR Hematology Ltd. Under the Invention Management Agreement, Dr. Charpentier retroactively consented to UC/Vienna's CRISPR/Cas9 license to Caribou as well as Caribou's sublicensing to Intellia certain of its rights to the UC/Vienna/Charpentier CRISPR/Cas9 intellectual property, subject to the restrictions of our license from Caribou. Under the agreement, the parties commit to maintain and coordinate the prosecution, defense and enforcement of the CRISPR/Cas9 foundational patent portfolio worldwide, and each of the co-owners of the intellectual property grants cross-consents to all existing and future licenses and sublicenses based on the rights of another co-owner. The Invention Management Agreement also includes retroactive approval by certain parties of certain prior assignments of interests in patent rights to other parties, and provides for, among other things, (i) good faith cooperation among the parties regarding patent maintenance, defense and prosecution, (ii) cost-sharing arrangements, and (iii) notice of and coordination in the event of third-party infringement of the subject patents. Unless earlier terminated by the parties, the Invention Management Agreement will continue in effect until the later of the last expiration date of the UC/Vienna/Charpentier patents underlying the CRISPR/Cas9 technology, or the date on which the last underlying patent application is abandoned.

Novartis In-Licensed Intellectual Property

Our December 2014 strategic collaboration and license agreement with Novartis grants us worldwide, non-exclusive, royalty-free rights to a portfolio of 14 Novartis patent families containing granted patents and pending applications in the United States and internationally relating to LNP compositions, methods of use and modified nucleic acids. The license permits us to use the Novartis LNPs to develop therapeutic, prophylactic, and palliative CRISPR-based *in vivo* products. The earliest claimed priority dates for the licensed patent families range from December 2009 through June 2013, and accordingly will expire by or after December 2030. The term of the license

continues until the expiration of the last-to-expire patent right that is licensed to either party. If we attempt to challenge any of the patents in the licensed families, Novartis may terminate the license on a patent-by-patent basis. We cannot guarantee that our products or delivery methods will be covered by issued claims in these families.

In addition, Novartis has also granted us rights to use its proprietary small molecule for HSC expansion. Our rights to this technology are subject to a single-digit royalty based on whether we develop and commercialize the relevant product solely or in collaboration with another third party.

Under our agreement with Novartis, any platform intellectual property developed as part of the collaboration is owned solely by us, while all other intellectual property developed within the collaboration, including product-based intellectual property, is jointly owned by us and Novartis. We cannot guarantee that intellectual property filed based on collaboration data will result in issued claims covering our products or delivery methods. Under our agreement with Novartis, we have also granted Novartis a sublicense to the intellectual property we license under our agreement with Caribou for the Novartis-selected HSC and CAR-T cells products, and *in vivo* products if applicable, with such sublicense being exclusive as long as Novartis uses commercially reasonable efforts to develop and commercialize those products.

Manufacturing

We currently have no commercial manufacturing or cell processing capabilities. We are exploring creating internal capabilities, as well as contracting qualified third-party organizations, to produce or process bulk compounds, formulated compounds, viral vectors or engineered cells for IND-supporting activities and early stage clinical trials. We expect that clinical and commercial quantities of any compound, vector, or engineered cells that we may seek to develop will be manufactured in facilities and by processes that comply with FDA and other regulations. At the appropriate time in the product development process, we will determine whether to establish our own manufacturing facilities or continue to rely on third parties to manufacture commercial quantities of any products that we may successfully develop.

Competition

The biotechnology industry is extremely competitive in the race to develop new products. While we believe we have significant competitive advantages with our industry-leading expertise in gene editing, clinical development expertise and dominant intellectual property position, we currently face and will continue to face competition for our development programs from companies that use genome editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities such as small molecules and antibodies. The competition is likely to come from multiple sources, including larger pharmaceutical companies, biotechnology companies and academia. Many of these competitors may have access to greater capital and resources than us. For any products that we may ultimately commercialize, not only will we compete with any existing therapies and those therapies currently in development, but we will also have to compete with new therapies that may become available in the future.

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

- genome editing companies focused on CRISPR/Cas9 including: Casebia Therapeutics, CRISPR Therapeutics, Inc., Editas Medicine, Inc., ToolGen, Inc. and Tracr Hematology Limited;
- other genome editing companies including: bluebird bio, Inc., Cellectis S.A., Homology Medicines, Inc., Poseida, Inc., Precision BioSciences, Inc., and Sangamo Therapeutics, Inc., and;
- genome therapy companies developing *in vivo* or *ex vivo* therapies, such as cell therapies, including: bluebird bio, Inc., Cellectis S.A., Celgene Corporation (which acquired Juno Therapeutics, Inc.), Gilead Sciences, Inc. (which acquired Kite Pharma, Inc.), Novartis A.G. and Spark Therapeutics, Inc.

Our competitors will also include companies that are or will be developing other genome editing methods as well as small molecules, biologics, *in vivo* gene therapies, *ex vivo* cell therapies and nucleic acid-based therapies for the same indications that we are targeting with our CRISPR/Cas9-based therapeutics.

Government Regulation and Product Approval

We are subject to extensive regulation. We expect our future *in vivo* and *ex vivo* product candidates to be regulated as biologics. Biological products are subject to regulation under the Food, Drug and Cosmetic (FD&C) Act and the Public Health Service Act (PHS Act), and other federal, state, local and foreign statutes and regulations. Both the FD&C Act and the PHS Act and their corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising and other promotional practices involving drug and biological products. Before clinical testing of biological products in the U.S. may begin, we must submit an IND to the FDA, which reviews the clinical protocol, and the IND must become effective before clinical trials may begin. We must also register our protocols with the National Institutes of Health (NIH) through its Recombinant DNA Advisory Committee (RAC) before initiating clinical testing and in some cases a public RAC review will be required.

Biologic products must be approved by the FDA before they may be legally marketed in the U.S. and by the appropriate foreign regulatory agencies before they may be legally marketed in foreign countries. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

Within the FDA, the Center for Biologics Evaluation and Research (CBER) regulates many biological products not regulated by the Center for Drug Evaluation and Research (CDER), including gene and cell therapies. Proposed human clinical trials involving nucleic acid transfer conducted at, or sponsored by, institutions receiving NIH funding for research with recombinant or synthetic nucleic acid molecules are also subject to review by the NIH RAC. Moreover, certain therapeutic protocols that raise important scientific, safety, medical, ethical, or social issues are discussed at the RAC's quarterly public meetings. While the FDA has not provided specific guidance on gene editing in humans, it has published guidance documents related to, among other things, gene therapy products in general, their preclinical assessment, observing subjects involved in gene therapy clinical trials for delayed adverse events, potency or other quality testing, and chemistry, manufacturing and control information in gene therapy INDs.

The FDA has provided guidance for the development of gene and cell therapy products that are relevant to the gene and cellular therapies we intend to develop. For example, the FDA has established the Office of Tissues and Advanced Therapies (OTAT) (previously known as Office of Cellular, Tissue and Gene Therapies) within CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee (CTGTAC) to advise CBER on its reviews. In addition, the FDA has issued a growing body of clinical, chemistry, manufacturing and control (CMC) guidance and other guidance, all of which are intended to facilitate industry's development of these products. More recently and as part of the implementation of the 21st Century Cures Act, FDA has issued a number of draft guidances pertaining to Regenerative Medicine Advanced Therapies, that include cell therapies and, as interpreted by FDA, "gene therapies including genetically modified cells, that lead to a durable modification of cells or tissues may meet the definition of a regenerative medicine therapy". A small number of gene therapy products have been approved by regulatory agencies. In 2012, the European Medicines Agency approved a gene therapy product called Glybera, which was the first gene therapy product approved by regulatory authorities anywhere in the Western world. And, in 2017, the FDA approved the first two cell-based gene therapy products

Ethical, social and legal concerns about gene-editing technology, gene therapy, genetic testing and genetic research could result in additional regulations restricting or prohibiting the processes we may use. Federal and state agencies, congressional committees and foreign governments have expressed interest in further regulating biotechnology. More restrictive regulations or claims that our products are unsafe or pose a hazard could prevent us from commercializing any product candidates. New government requirements may be established that could delay or prevent regulatory approval of our product candidates under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be.

U.S. Drug and Biological Products Development Process

The FDA approves drugs through the New Drug Application (NDA) process and biologics through the Biologics License Application (BLA) process before they may be legally marketed in the U.S. This process generally involves the following:

- completion of extensive nonclinical, sometimes referred to as preclinical laboratory tests, and preclinical animal studies and applicable requirements for the humane use of laboratory animals and formulation studies in accordance with applicable regulations, including good laboratory practice (GLP);
- submission to the FDA of an IND application, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as good clinical practice (GCP) and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed product for its intended use;
- submission to the FDA of an NDA or BLA for marketing approval that includes substantial evidence of safety and efficacy or, for biological products, safety, purity, and potency, from nonclinical testing and clinical trials;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the product is produced to assess compliance with current good manufacturing practice (cGMP) to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity and, if applicable, the FDA's current good tissue practice (cGTP) requirements for the use of human cellular and tissue products;
- positive results from potential FDA audit of the nonclinical study and clinical trial sites that generated the data in support of the NDA or BLA; and
- FDA review and approval of the NDA or licensure of the BLA.

Before testing any drug or biological product candidate in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLP.

Where a study involving the transfer of nucleic acids into humans is conducted at, or sponsored by, institutions receiving NIH funding for recombinant DNA research or synthetic nucleic acid molecules, prior to the submission of an IND to the FDA, a protocol and related documentation is submitted to and the study is registered with the NIH Office of Biotechnology Activities (OBA), pursuant to the NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines). Compliance with the NIH Guidelines is mandatory for investigators at institutions receiving NIH funds for research involving recombinant DNA; however, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. The NIH is responsible for convening the RAC, a federal advisory committee that reviews research proposals involving human-gene transfer research and discusses, if needed, protocols that raise novel or particularly important scientific, safety or ethical considerations. The RAC decides whether a protocol raises issues that warrant further discussion at its quarterly meetings, and the OBA will notify the FDA of the RAC's decision regarding the necessity for full public review of a particular protocol. RAC proceedings and reports are posted to the OBA web site and may be accessed by the public.

The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. With gene therapy protocols, if the FDA allows the IND to proceed, but the RAC decides

that full public review of the protocol is warranted, the FDA will request at the completion of its IND review that sponsors delay initiation of the protocol until after completion of the RAC review process. The FDA may also impose clinical holds on a drug or biological product candidate at any time before or during clinical trials due to, among other reasons, safety concerns or non-compliance with regulatory requirements. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that result in the suspension or termination of such trials.

Clinical trials involve the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the study sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical trial must be reviewed and approved by an independent institutional review board (IRB) at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of study participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Certain clinical trials also must be reviewed by an institutional biosafety committee (IBC), a local institutional committee that reviews all forms of research conducted at that institution involving recombinant or synthetic nucleic acid molecules. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment and ensures that all research is conducted in compliance with NIH Guidelines.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase I. The product candidate is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase II. The product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase III. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency (for BLA products), and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product approval and labeling.

Post-approval clinical trials, sometimes referred to as Phase IV clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. The FDA typically advises that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by ten years of annual queries, either in person or by questionnaire.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the status of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, the NIH and the investigators for serious and unexpected adverse events, any findings from other trials, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening

suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase I, Phase II and Phase III clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products, including drugs and biologics, are required to register and disclose certain clinical trial information to NIH. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made publicly available as part of the registration at www.clinicaltrials.gov. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved, up to a maximum of two years.

Human therapeutic products based on gene-editing technology are a new category of therapeutics. Because this is a relatively new and expanding area of novel therapeutic interventions, there can be no assurance as to the length of the study period, the number of patients the FDA will require to be enrolled in the trials in order to establish the safety and efficacy for NDA products and the safety, purity and potency for BLA products that are human gene editing therapeutics, or that the data generated in these trials will be acceptable to the FDA to support marketing approval. The NIH and the FDA have a publicly accessible database, the Genetic Modification Clinical Research Information System, which includes information on gene transfer trials and serves as an electronic tool to facilitate the reporting and analysis of adverse events in these trials.

Concurrent with clinical trials, companies usually complete additional animal trials and must also develop additional information about the physical characteristics of the product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP, and in certain cases, cGTP, requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHS Act emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final product, if approval is sought under a BLA, and testing methods to demonstrate that the drug's quality is adequate to preserve the drug's identity, strength, quality and purity, if approval is sought under an NDA. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

After the completion of clinical trials of a drug or biological product candidate, FDA approval of an NDA or BLA must be obtained before commercial marketing of the drug or biological product. The NDA or BLA must include results of product development, laboratory and animal trials, human trials, information on the manufacture and composition of the product, proposed labeling and other relevant information. In addition, under the Pediatric Research Equity Act (PREA), an NDA, BLA or supplement to an NDA or BLA for a product candidate with certain novel characteristics must contain data to assess the safety and effectiveness of the product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The Food and Drug Administration Safety and Innovation Act (FDASIA) requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan (PSP) within sixty days after an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. The initial PSP must include, among other things, an outline of the pediatric study or studies that the sponsor plans to conduct, including, to the extent practicable, study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information, along with any other information specified in FDA regulations. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to

an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, or other clinical development programs. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug or biological product for an indication for which orphan designation has been granted. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the NDA or BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Under the Prescription Drug User Fee Act (PDUFA), as amended, each NDA or BLA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs or BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews an NDA or BLA to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any NDA or BLA that it deems incomplete or not properly reviewable at the time of submission, including for failure to pay required fees, and may request additional information. In this event, the application must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA or BLA. The FDA reviews the application to determine, among other things, whether the proposed product is safe and effective (or, in the case of biological products, safe, pure and potent), and whether the product is being manufactured in accordance with cGMP, and in certain cases, cGTP, requirements to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel products or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the FDA review and approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy (REMS) is necessary to assure the safe use of the drug or biological product candidate. If the FDA concludes a REMS is needed, the sponsor of the NDA or BLA must submit a proposed REMS; the FDA will not approve the application without a REMS, if required.

Before approving an NDA or BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP and, if applicable, cGTP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements and cGCP requirements. To assure cGMP, cGTP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the NDA or BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the NDA or BLA in its present form, the FDA will issue a complete response letter that usually describes all of the specific deficiencies in the application identified by the FDA. The deficiencies identified may be minor, for example, requiring clarifying labeling changes, or major, for example, requiring product reformulation or additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the application, addressing all of the deficiencies identified in the letter, challenge the determination set forth in the letter by requesting a hearing or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases, dosages or patient subgroups or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings, precautions or adverse events be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a REMS, or otherwise limit the scope of any approval. In addition, the FDA

may require post marketing clinical trials, sometimes referred to as Phase IV clinical trials, designed to further assess a product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

One of the performance goals agreed to by the FDA under the PDUFA is to review 90% of BLAs in 10 months from the 60-day filing date, and 90% of priority BLAs in six months from the 60-day filing date, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change with PDUFA reauthorization. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Orphan Drug Designation

The FDA may grant Orphan Drug Designation to drugs or biological products intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the U.S., or, if it affects more than 200,000 individuals in the U.S., when there is no reasonable expectation that the cost of developing and marketing the drug or biological product for this type of disease or condition will be recovered from sales in the U.S. Orphan product designation must be requested before submission of an NDA or BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

In the U.S., Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same orphan indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer with orphan exclusivity is unable to assure sufficient quantities of the approved orphan designated product. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity, which may permit off-label use for the orphan indication. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug or biological product as defined by the FDA for the same orphan indication or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity.

Expedited Development and Review Programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drug and biological products that meet certain criteria. Specifically, new drug and biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request that the FDA designate the product as a Fast Track product at any time during the clinical development of the product, but ideally not later than the pre-NDA or pre-BLA meeting. The FDA may consider for review sections of the marketing application for a Fast Track product on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness of the treatment, prevention, or diagnosis of that condition. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological

product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Drug and biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a product subject to accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

In addition, under the provisions of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA), the FDA established a Breakthrough Therapy Designation, which is intended to expedite the development and review of products that treat serious or life-threatening diseases or conditions. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the features of Fast Track designation, as well as more intensive FDA interaction and guidance. The Breakthrough Therapy Designation is a distinct status from both accelerated approval and priority review, but these can also be granted to the same product candidate if the relevant criteria are met. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. All requests for breakthrough therapy designation will be reviewed within 60 days of receipt, and FDA will either grant or deny the request.

Fast Track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process. Where applicable, we plan to request Fast Track and Breakthrough Therapy Designation for our product candidates. Even if we receive one or both of these designations for our product candidates, the FDA may later decide that our product candidates no longer meet the conditions for qualification. In addition, these designations may not provide us with a material commercial advantage.

Regenerative medicine advanced therapies (RMAT) designation

As part of the 21st Century Cures Act, the FD&C Act was amended to facilitate an efficient development program for, and expedite review of regenerative medicine advanced therapies, which include cell and gene therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products. This program is intended to facilitate efficient development and expedite review of regenerative medicine therapies, which are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and qualify for RMAT designation. A drug sponsor may request that FDA designate a drug as a RMAT concurrently with or at any time after submission of an IND. FDA has 60 calendar days to determine whether the drug meets the criteria, including whether there is preliminary clinical evidence indicating that the drug has the potential to address unmet medical needs for a serious or life-threatening disease or condition. A BLA for a regenerative medicine therapy that has received RMAT designation may be eligible for priority review or accelerated approval through use of surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites. Benefits of RMAT designation also include early interactions with FDA and for those granted accelerated approval post-approval requirements may be fulfilled through the submission of clinical evidence from clinical studies, patient registries, or other sources of real world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval.

Post-Approval Requirements

Maintaining substantial compliance with applicable federal, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Rigorous and extensive FDA regulation of drug and

biological products continues after approval, particularly with respect to cGMP requirements. We will rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of certain components of products that we may commercialize. Manufacturers of our products are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to drug and biological products, include reporting of cGMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record-keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, and complying with electronic record and signature requirements. After a BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products.

We also would have to comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet and social media platforms. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the labeling or marketing of a product, imposition of a REMS or post-market study requirement or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Drug and biological product manufacturers and other entities involved in the manufacture and distribution of approved drugs and biological products are required to register their establishments with the FDA and certain other federal and state agencies, and are subject to periodic unannounced inspections by the FDA and certain other federal and state agencies for compliance with cGMP, and in certain cases, cGTP, requirements and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA or BLA, including withdrawal of the product from the market. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA plus the time between the submission date of an NDA or BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent within a 60-day period from the date the product is first approved for commercial marketing. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term

extension or restoration. In the future, we may intend to apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA. However, there can be no assurance that any such extension will be granted to us.

Under Hatch-Waxman Act, once an NDA is approved, potential competitors can rely upon the NDA upon expiration of certain patent and non-patent exclusivity periods, if any, to seek approval of competing products, including generic copies, via an abbreviated new drug application, or ANDA, or 505(b)(2) application. Both the ANDA and 505(b)(2) application processes allow a competitor to obtain approval without conducting all of the preclinical and clinical testing necessary for approval of a full NDA, which could result in a shorter and less expensive development and approval process.

The Hatch-Waxman Act provides for various periods of non-patent exclusivity to protect new drugs approved via a full NDA from premature competition. First, federal law provides a period of up to five years exclusivity following approval of a drug containing a new chemical entity, or NCE, defined as an active moiety that has not been approved previously. An active moiety, in turn, is defined as the molecule or ion responsible for the action of the drug substance. During this NCE exclusivity period, FDA cannot accept any ANDA or 505(b)(2) application referencing the NDA of the protected listed drug; however, the five-year exclusivity period is reduced to four years if the ANDA or 505(b)(2) application challenges to a listed patent for the protected drug product through submission of a paragraph IV certification (described below). Second, the Hatch-Waxman Act also provides for a period of three years of exclusivity following approval of a listed drug that contains a previously approved active ingredient if the FDA determines that new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are essential to the approval of the application. Three-year exclusivity is typically awarded for changes to an approved drug product, such as new indications, dosage forms or dosing regimens, and prohibits FDA from approving an ANDA or 505(b)(2) application with the protected innovation. As a general matter, three-year exclusivity does not prohibit the FDA from approving ANDAs or 505(b)(2) applications for competitive versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Additionally, in the event that the sponsor of the listed drug has properly informed the FDA of patents covering its listed drug, applicants submitting an ANDA or 505(b)(2) application referencing the listed drug are required to make one of four patent certifications for each listed patent, except for patents covering methods of use for which the ANDA or 505(b)(2) applicant is not seeking approval. If an applicant certifies its belief that one or more listed patents are invalid, unenforceable, or not infringed (and thereby indicates it is seeking approval prior to patent expiration), which is known as a paragraph IV certification, it is required to provide notice of its filing to the NDA sponsor and the patent holder within certain time limits. If the patent holder then initiates a suit for patent infringement against the ANDA or 505(b)(2) applicant within 45 days of receipt of the notice, the FDA cannot grant effective approval of the ANDA or 505(b)(2) application until either 30 months have passed or there has been a court decision or settlement order holding or stating that the drug for which approval is being sought will not infringe the patents in question or that the patents are invalid or unenforceable. If the patent holder does not initiate a suit for patent infringement within the 45 days, the ANDA or 505(b)(2) application may be approved immediately upon successful completion of FDA review, unless blocked by another listed patent or regulatory exclusivity period. If the ANDA or 505(b)(2) applicant certifies that it does not intend to market its generic product before some or all listed patents on the listed drug expire (known as a Paragraph III certification), then the FDA cannot grant effective approval of the ANDA or 505(b)(2) application until those patents expire. The first of the ANDA applicants submitting substantially complete applications certifying that one or more listed patents for a particular product are invalid, unenforceable, or not infringed may qualify for an exclusivity period of 180 days running from when the generic product is first marketed, during which subsequently submitted ANDAs containing similar certifications cannot be granted effective approval. The 180-day generic exclusivity can be forfeited in various ways, including if the first applicant does not market its product within specified statutory timelines. If more than one applicant files a substantially complete ANDA on the same day, each such first applicant will be entitled to share the 180-day exclusivity period, but there will only be one such period, beginning on the date of first marketing by any of the first applicants.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the Affordable Care Act), signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 (BPCIA), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Starting in 2015, the FDA commenced licensing biosimilars under the BPCIA, and there are currently numerous biosimilars approved in the U.S. and Europe. The FDA has issued several draft and final guidance documents outlining an approach to review and approval of biosimilars and interchangeable biological products.

The BPCIA also contains various provisions regarding exclusivity for reference and interchangeable products and procedures for sharing and litigating patents covering the reference product. The BPCIA, however, is complex and only beginning to be interpreted and implemented by the FDA. In addition, proposed legislation has sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and meaning of the BPCIA is subject to significant uncertainty.

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, all affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

Other Healthcare Laws

In addition to FDA restrictions on marketing of pharmaceutical and biological products, other U.S. federal and state healthcare regulatory laws restrict business practices in the pharmaceutical industry, which include, but are not limited to, state and federal anti-kickback, false claims, data privacy and security, and physician payment transparency laws.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting, receiving or providing any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not meet the requirements of a statutory or regulatory exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. Penalties for violations of the Anti-Kickback Statute include fines of up to $25,000 per violation and felony conviction punishable by imprisonment up to five years as well as possible exclusion from participation in federal healthcare programs, such as Medicare and Medicaid.

We may also be subject to data privacy and security regulation by both the federal government and the states and other jurisdictions outside the U.S. in which we conduct our business. HIPAA, as amended by the Health

Information Technology for Economic and Clinical Health Act (HITECH) and their respective implementing regulations, including the Final HIPAA Omnibus Rule published on January 25, 2013, impose specified requirements relating to the privacy, security and transmission of individually identifiable health information held by covered entities and their business associates. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same requirements, thus complicating compliance efforts.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and individual imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

To the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act, to which we are subject, prohibits corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity.

Government Regulation Outside of the United States

In addition to regulations in the U.S., we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical studies and any commercial sales and distribution of our products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological product for which we obtain regulatory approval. In the U.S. and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of any products for which we receive regulatory approval for commercial sale will therefore depend, in part, on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations.

The process for determining whether a third-party payor will provide coverage for a pharmaceutical or biological product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. A decision by a third-party payor not to cover our product

candidates could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Moreover, a third-party payor's decision to provide coverage for a pharmaceutical or biological product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Additionally, coverage and reimbursement for new products can differ significantly from payor to payor. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor separately and will be a time-consuming process.

The containment of healthcare costs has become a priority of federal, state and foreign governments as well as private third-party payors, and the prices of pharmaceutical or biological products have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost-effectiveness of pharmaceutical products, biological products, medical devices and medical services, in addition to questioning safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after FDA approval or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit.

Employees

As of February 28, 2018, we had 195 full-time employees, 152 of whom were primarily engaged in research and development activities and 68 of whom have an M.D. or Ph.D. degree.

Our Corporate Information

We were incorporated under the laws of the state of Delaware in May 2014 under the name AZRN, Inc. Our principal executive offices are located at 40 Erie Street Suite 130, Cambridge, Massachusetts 02139. Our telephone number is (857) 285-6200, and our website is located at www.intelliatx.com. References to our website are inactive textual references only and the content of our website should not be deemed incorporated by reference into this Annual Report on Form 10-K.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, are available free of charge on our website located at www.intelliatx.com as soon as reasonably practicable after they are filed with or furnished to the Securities and Exchange Commission (the "SEC"). These reports are also available at the SEC's Internet website at www.sec.gov. The public may also read and copy any materials filed with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Washington D.C. 20549. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330.

A copy of our Corporate Governance Guidelines, Code of Conduct and Business Ethics and the charters of the Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are posted on our website, www.intelliatx.com, under "Investor Relations".

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 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. 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, CRISPR-based genome editing technologies are relatively new, and their therapeutic utility is largely unproven. The CRISPR/Cas9 technologies 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 technologies. The scientific evidence to support the feasibility of developing products based on these technologies 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 and efficacy 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 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 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 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 or 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 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, clinical and 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 effectiveness 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, they may not receive regulatory approval.

Our approach to developing therapies for genetic and viral-based diseases 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 this category of *in vivo* therapeutics, including preclinical and clinical requirements for approval of an IND;
- educating medical personnel 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 acceptance.

Additionally, because our *in vivo* technology involves gene editing across multiple cell and tissue types, we are subject to many of the challenges and risks that gene therapies face, including:

- regulatory guidance regarding the requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. To date, no products that involve the *in vivo* genetic modification of patient cells have been approved in the U.S. and a limited number have been approved in the EU;
- improper insertion of a gene sequence into a patient's chromosome could lead to cancer, other aberrantly functioning cells or other diseases, including death;
- the FDA recommends a follow-up observation period of 15 years or longer for all patients who receive treatment using gene therapies, and we may need to adopt such an observation period for our product candidates; and
- clinical trials using therapies that genetically modify cells conducted at institutions that receive funding for recombinant DNA research from the NIH, may be subject to review by the RAC. Although the FDA decides whether individual protocols may proceed, the RAC review process can impede the initiation of a clinical trial, even if the FDA has reviewed the study and it has become effective under an IND.

Further, because our *ex vivo* product candidates involve gene editing human cells and then manufacturing and delivering modified cells to patients, we are subject to many of the challenges and risks that cell therapies face, including:

- clinical trials using genetically modified cells conducted at institutions that receive funding for recombinant DNA research from the NIH, may be subject to review by the RAC. Although the FDA

decides whether individual protocols may proceed, the RAC review process can impede the initiation of a clinical trial, even if the FDA has reviewed the study and it has become effective under an IND; and

- clinical trials using engineered cell therapies require unique products to be created for each patient and such individualistic manufacturing may be both inefficient and cost-prohibitive.

To date, although human clinical trials for other *in vivo* genome editing-based therapeutics have been authorized by the FDA, neither we nor any other company has received regulatory approval in the U.S. or EU to commence human clinical trials utilizing *in vivo* CRISPR/Cas9-based therapeutics or to market *in vivo* therapeutics utilizing any genome editing technology, including CRISPR/Cas9. 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 *in vivo* genome editing-based 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 *in vivo* genome editing-based therapeutics. In addition, if any product candidates encounter safety or efficacy problems, developmental delays, regulatory issues or other problems, our development plans and business could be significantly harmed. Further, competitors that are developing *in vivo* 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 significantly modify the current legal framework governing the FDA. Any such changes to the FDA requirements could impact our ability to obtain approval for our products or sell them profitably. In addition, in the EU, the decision of the United Kingdom to withdraw from the European Union 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 have commenced human trials involving *in vivo* CRISPR/Cas9-based therapeutics in China. Neither these entities nor the Chinese regulatory agencies have shared publicly any specific any information on the regulatory process for clinical trial approval including any 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 gene 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 off-target editing or immunogenicity;
- 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 gene 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 in vivo CRISPR/Cas9 use, gene 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 gene editing in particular, remain novel technologies, with the first gene therapy product being approved in August 2017 in the U.S. and only a limited number of gene therapy products approved to date in the EU. Public perception may be influenced by claims that gene therapy or gene editing, including the use of CRISPR/Cas9, is unsafe or unethical, and gene therapy or gene 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, and the FDA recently initiated a clinical hold on a CAR-T cell therapy clinical trial due to patient deaths, and the company developing the therapy ultimately decided to stop the program. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy or gene 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 gene 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.

We have not currently selected any particular product candidates for clinical development. 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 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 pre-clinical studies are not necessarily predictive of our other ongoing and future pre-clinical 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 pre-clinical or clinical studies, we may be unable to successfully develop, obtain regulatory approval for and commercialize any potential product candidate.

There is a high failure rate for product candidates progressing through pre-clinical and clinical studies. Even if we are able to successfully complete our ongoing and future pre-clinical studies for any potential product candidate, we may not be able to replicate any positive results from these or any other studies in any of our future pre-clinical 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 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 pre-clinical and clinical 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 non-human primate studies are based on top-line interim data and may ultimately differ from actual results once additional data are received and fully evaluated.

The reported results of the non-human primate studies that we have publicly disclosed, and that are discussed herein and in documents we incorporated by reference, consist of top-line interim data. Top-line interim data are based on a preliminary analysis of currently-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 a comprehensive review of the more extensive data that we expect to receive related to the studies. Our reported results and related top-line interim data are based on assumptions, estimations, calculations and information currently available to us, and we have not received or had an opportunity to fully evaluate all of the data related to the studies. As a result, the top-line interim data results that we have reported may differ from future results, or different conclusions or considerations may qualify such results, once the current data or additional data have been received and fully evaluated. 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 top-line interim data that we have reported related to non-human primate differ from actual results or is perceived as insufficient or faulty, our ability to 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 NDA or 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 (IRBs) or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations (CROs), the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of any product candidates may fail to show safety or efficacy, produce negative or inconclusive results and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon product development programs;
- the number of patients required for clinical trials of any product candidates may be larger than we anticipate, enrollment in these clinical trials may be lower than required by the regulatory agencies or slower than we anticipate, or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of preclinical studies and clinical trials of any product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators, IRBs or ethics committees to suspend or terminate the trials, or reports may arise from preclinical or clinical testing of other gene therapies or gene editing based therapies that raise safety or efficacy concerns about our product candidates; and
- the FDA or other regulatory authorities may require us to submit additional data, such as long-term toxicology studies, or impose other requirements before permitting us to initiate or rely on a clinical trial.

We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, the Data Safety Monitoring Board (DSMB) for such trial or FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by FDA or other regulatory authorities resulting in the imposition of a clinical hold, manufacturing or quality control issues, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product or treatment, failure to establish or achieve clinically meaningful trial endpoints, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials.

Our product development costs will increase if we experience delays in clinical testing or marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be

restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates and may allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations. Any delays in our preclinical or future clinical development programs may harm our business, financial condition and prospects significantly.

Inconclusive results, lack of efficacy, adverse events or additional safety concerns in clinical trials that we or others conduct may impede the regulatory approval process or overall market acceptance of our future product candidates.

Therapeutic applications of gene editing technologies, and CRISPR/Cas9 in particular, for both *in vivo* products and utilization in engineered cell therapies, are unproven and must undergo rigorous clinical trials and regulatory review before receiving marketing authorization. If the results of our clinical studies or those of any other third parties, including with respect to gene editing technology or engineered cell therapies, are inconclusive, fail to show efficacy or if such clinical trials give rise to safety concerns or adverse events, we may:

- be delayed in obtaining marketing approval for our future product candidates, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to the addition of labeling statements, such as warnings or contraindications, or other types of regulatory restrictions or scrutiny;
- be subject to changes in the way the product is administered;
- be required to perform additional clinical studies to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities modify or withdraw their legal requirements or written guidance, if any, regarding the applicable regulatory approval pathway or any approval of the product in question, or impose restrictions on its distribution in the form of a modified REMS;
- be sued; or
- experience damage to our reputation.

Additionally, our future product candidates could potentially cause other adverse events that have not yet been predicted and the potentially permanent nature of gene editing effects, including CRISPR/Cas9's effects, on genes or novel cell therapies in the organs of the human body may make these adverse events irreversible. The inclusion of critically ill patients in our clinical studies or those of our competitors may result in deaths or other adverse medical events, including those due to other therapies or medications that such patients may be using. Any of these events could prevent us from achieving or maintaining regulatory approval or market acceptance of our future product candidates and impair our ability to achieve profitability.

We have never generated any revenue from product sales and our ability to generate revenue from product sales and become profitable depends significantly on our success in a number of areas.

We have no products approved for commercial sale, have not generated any revenue from product sales, and do not anticipate generating any revenue from product sales until sometime after we have received regulatory approval for the commercial sale of a product candidate that we discover. Our ability to generate revenue and achieve and retain profitability depends significantly on our success in many areas, including:

- selecting commercially viable product candidates and effective delivery methods;
- completing research, preclinical and clinical development of product candidates;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we complete clinical trials;

- developing a sustainable and scalable manufacturing process for product candidates, including establishing and maintaining commercially viable supply relationships with third parties and potentially establishing our own manufacturing capabilities and infrastructure;
- launching and commercializing product candidates for which we obtain regulatory approvals and marketing authorizations, either directly or with a collaborator or distributor;
- accurately assessing the size and addressability of potential patient populations;
- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter or which may be necessary for us to develop, manufacture or commercialize our product candidates;
- maintaining good relationships with our collaborators and licensors;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- avoiding infringement of or obtaining licenses to any valid intellectual property owned or controlled by third parties; and
- attracting, hiring and retaining qualified personnel.

Even if one or more product candidates that we discover and develop are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate and the timing of such costs may be out of our control. Our expenses could increase beyond expectations if we are required by the FDA or other regulatory agencies, domestic or foreign, to change our manufacturing processes or assays, or to perform clinical, nonclinical or other types of additional studies. If we are successful in obtaining regulatory approvals to market one or more product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price and whether we own the commercial rights for that territory. If the number of our addressable disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. If we are not able to generate revenue from the sale of any approved products, we may never become profitable.

We face significant competition in an environment of rapid technological change. The possibility that our competitors may achieve regulatory approval before we do or develop therapies that are more advanced or effective than ours may harm our business and financial condition or our ability to successfully market or commercialize our product candidates.

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

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

- genome editing companies focused on CRISPR/Cas9 including: Casebia Therapeutics, CRISPR Therapeutics, Inc., Editas Medicine, Inc., ToolGen, Inc. and Tracr Hematology Limited;
- other genome editing companies including: bluebird bio, Inc., Cellectis S.A., Homology Medicines, Inc., Poseida, Inc., Precision BioSciences, Inc. and Sangamo Therapeutics, Inc.; and
- genome therapy companies developing *in vivo* or *ex vivo* therapies, such as cell therapies, including: bluebird bio, Inc., Cellectis S.A., Celgene Corporation (which acquired Juno Therapeutics, Inc.), Gilead Sciences, Inc. (which acquired Kite Pharma, Inc.), Novartis A.G. and Spark Therapeutics, Inc.

Our competitors will also include companies that are or will be developing other genome editing methods as well as small molecules, biologics, *in vivo* gene therapies, *ex vivo* cell therapies and nucleic acid-based therapies for the same indications that we are targeting with our CRISPR/Cas9-based therapeutics.

Any advances in gene therapy, cell therapies or gene editing technology made by a competitor may be used to develop therapies that could compete against any of our product candidates. Many of these competitors have substantially greater research and development capabilities and financial, scientific, technical, intellectual property, manufacturing, marketing, distribution and other resources than we do, and we may not be able to successfully compete with them.

To become and remain profitable, we must discover, develop and eventually commercialize product candidates with significant market potential, which will require us to be successful in a range of challenging activities. These activities can include completing preclinical studies and clinical trials of product candidates, obtaining marketing approval for product candidates, manufacturing, marketing and selling products that are approved and satisfying any post-marketing requirements. Even if we are successful in selecting and developing any product candidates, in order to compete successfully we may need to be first-to-market or demonstrate that our CRISPR/Cas9-based products are superior to therapies based on the same or different treatment methods. If we are not first-to-market or are unable to demonstrate such superiority, any products for which we are able to obtain approval may not be successful. Furthermore, in certain jurisdictions, if a competitor has orphan drug status for a product and if our product candidate is determined to be contained within the scope of a competitor's orphan drug exclusivity, then approval of our product for that indication or disease could potentially be blocked, for example, for up to seven years in the U.S. and 10 years in the EU.

We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of the Company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations.

We have a very limited operating history, which may make it difficult to evaluate our current business and predict our future performance.

We are very early in our development efforts and all of our lead programs are still in the discovery stage. We were formed in May 2014, have no products approved for commercial sale and have not generated any revenue from product sales. Our ability to generate product revenue or profits, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. We may never be able to develop or commercialize a marketable product.

Each of our programs may require additional discovery research and then preclinical and clinical development, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. In addition, our product candidates must be approved for marketing by the FDA or certain other foreign regulatory agencies, including the EMA, before we may commercialize any product.

Our limited operating history, particularly in light of the rapidly evolving gene editing field, may make it difficult to evaluate our current business and predict our future performance. Our very short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by very early stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

We have incurred net losses in each period since our inception, anticipate that we will continue to incur net losses in the future and may never achieve profitability.

We are not profitable and have incurred losses in each period since our inception. Our net loss was $67.5 million for the year ended December 31, 2017. As of December 31, 2017, we had an accumulated deficit of $121.1 million. We expect these losses to increase as we continue to incur significant research and development and other expenses related to our ongoing operations, seek regulatory approvals for our future product candidates, scale-up manufacturing capabilities, maintain, expand and protect our intellectual property portfolio and hire additional personnel to support the development of our product candidates and to enhance our operational, financial and information management systems.

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

We may need to raise substantial additional funding to fund our operations. If we fail to obtain additional financing, we may be unable to complete the development and commercialization of any product candidates.

Our operations have required substantial amounts of cash since inception, and we expect to spend substantial amounts of our financial resources on our discovery programs going forward and future development efforts. If we are able to identify product candidates that are eventually approved, we will require significant additional amounts in order to launch and commercialize our product candidates. For the foreseeable future, we expect to continue to rely on additional financing to achieve our business objectives.

We will require additional capital for the further development and commercialization of any product candidates and may need to raise additional funds sooner if we choose to expand more rapidly than we presently anticipate or due to other unanticipated factors.

We cannot be certain that additional funding will be available on acceptable terms, or at all. We have no committed source of additional capital and if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. Our collaboration and license agreements may also be terminated if we are unable to meet the payment or other obligations under the agreements. We could be required to seek collaborators for product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

Raising additional capital may cause dilution to our stockholders and restrict our operations.

We will need additional capital in the future to continue our planned operations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our ability to complete clinical trials or our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for any future product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the U.S. If patients are unwilling to participate in our clinical studies because of concerns about, or negative publicity from, adverse events in the gene editing field, the novel nature of the CRISPR/Cas9 gene editing technology, the irreversibility of the effects of CRISPR/Cas9 or for other reasons, including competitive clinical studies for similar patient populations, then the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical studies altogether. In addition, any patients who would otherwise be eligible for clinical trials that we may hold may instead enroll in clinical trials of product candidates of our competitors.

Patient enrollment is affected by other factors including:

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

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

We expect to expand our research, development and regulatory capabilities, and, as a result, we may encounter difficulties in hiring capable personnel and otherwise managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of technology research, product development and manufacturing, clinical and regulatory affairs and, if any product candidates are submitted for or receive marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to recruit and train additional qualified personnel or to

otherwise effectively manage the expansion of our operations. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business and development plans or disrupt our operations.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical, legal, financial and business development expertise of John M. Leonard, M.D., our President and Chief Executive Officer, Graeme Bell, our Executive Vice President, Chief Financial Officer, and José E. Rivera, our Executive Vice President, General Counsel, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment arrangements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

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

If, in the future, we are unable to establish sales, marketing and distribution capabilities or enter into agreements with third parties to sell, market and distribute products based on our technologies, we may not be successful in commercializing our products if and when any products candidates or therapies are approved and we may not be able to generate any revenue.

We do not currently have a sales, marketing or distribution infrastructure and, as a company, have no experience in the sale, marketing or distribution of therapeutic products. To achieve commercial success for any approved product candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if they are approved.

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

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future product candidates that we may develop;

- the lack of complementary treatments to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- the location of patients in need of our product candidates and the treating physicians who may prescribe the products; and
- unforeseen costs and expenses, as well as legal and regulatory requirements, associated with creating and operating a sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability to us from these revenue streams is likely to be lower than if we were to market and sell any product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we may not be successful in commercializing our product candidates. Further, our business, results of operations, financial condition and prospects will be materially adversely affected.

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

In December 2014, we entered into a collaboration agreement with Novartis regarding the discovery of new CRISPR/Cas9-based therapies principally using CAR-T cells and HSCs. Under the Novartis collaboration agreement, we received a commitment to advance multiple programs. Pursuant to the Novartis agreement, we granted Novartis exclusive rights to further develop and commercialize products arising out of the CAR-T cell program during the research term. Regarding HSCs, we are jointly advancing multiple programs with Novartis and have agreed to a process for assigning development and ownership rights, which may enable us to develop our own proprietary HSC pipeline.

In April 2016, we entered into a collaboration agreement with Regeneron that includes a product component to research, develop and commercialize CRISPR/Cas-based therapeutic products primarily focused on gene editing in the liver as well as a technology collaboration component, pursuant to which we and Regeneron will engage in research and development activities aimed at discovering and developing novel technologies and improvements to CRISPR/Cas technology to enhance our gene editing platform. Pursuant to the Regeneron collaboration agreement, we granted Regeneron exclusive rights to select up to 10 targets, subject to certain restrictions, while we retain the rights to solely develop our initial indications, other than ATTR, which will be subject to a co-development and co-commercialization arrangement with Regeneron, and have the right to choose additional liver targets for our own development during the collaboration term. Certain other of the development targets under the Regeneron agreement may also be subject to a co-development/co-commercialization arrangement with the other party at the other party's option.

Either Novartis or Regeneron may change its strategic focus or pursue alternative technologies in a manner that results in reduced, delayed or no revenue to us. Each of Novartis and Regeneron has a variety of marketed products and product candidates either by itself or under collaboration with other companies, including some of our competitors, and the respective corporate objectives of Novartis or Regeneron may not be consistent with our best interests. If either of our collaboration partners fails to develop, obtain regulatory approval for or ultimately commercialize any product candidate from the development programs governed by the respective collaboration agreement in the applicable territories, or if either of our collaboration partners terminates our collaboration with it, our business, financial condition, results of operations and prospects could be harmed. In addition, any dispute or litigation proceedings we may have with either Novartis or Regeneron in the future could delay development programs, create uncertainty as to ownership of or access to intellectual property rights, distract management from other business activities and generate substantial expense.

Our existing and future collaborations will be important to our business. If we are unable to maintain any of these collaborations, or if these collaborations are not successful, our business could be adversely affected.

We have limited capabilities for product discovery and development and do not yet have any capability for sales, marketing or distribution. Accordingly, we have entered, and plan to enter, into collaborations with other companies, including our therapeutic-focused collaboration agreements with Novartis and Regeneron, that we believe can provide such capabilities. These therapeutic-focused collaborations provide us with important technologies and funding for our programs and technology, and we expect to receive additional technologies and funding under these and other collaborations in the future. Our existing therapeutic collaborations, and any future collaborations we enter into, may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs or license arrangements based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as a strategic transaction that may divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could develop independently or with third parties products that compete directly or indirectly with our products and product candidates if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the development or commercialization of our product candidates;
- collaborators may fail to comply with applicable legal and regulatory requirements regarding the development, manufacture, sale, distribution or marketing of a product candidate or product;
- collaborators with sale, marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the sale, marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation, payment obligations or the preferred course of discovery, development, sales or marketing, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional and burdensome responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend their or our relevant intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation and liability;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- if a collaborator of ours is involved in a business combination or cessation, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us; and
- collaborations may be terminated by the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If our therapeutic collaborations do not result in the successful discovery, development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development and commercialization of our technology and product candidates could be delayed and we may need additional resources to develop product candidates and our technology. All of the risks relating to product discovery, development, regulatory approval and commercialization described in this report also apply to the activities of our therapeutic collaborators.

Additionally, if one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

For some of our programs, we may in the future determine to collaborate with pharmaceutical and biotechnology companies for discovery, development and potential commercialization of therapeutic products. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail discovery efforts or the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake discovery, development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary discovery, development and commercialization activities, we may not be able to further develop our product candidates, bring them to market or continue to develop our technology and our business may be materially and adversely affected.

Gene editing products and engineered cell therapies are novel and may be complex and difficult to manufacture. We could experience manufacturing problems that result in delays in the development or commercialization of our product candidates or otherwise harm our business.

The manufacturing process used to produce CRISPR/Cas9-based *in vivo and ex vivo* product candidates, including engineered cell therapies, may be complex, as they are novel and have not been validated for clinical and commercial production. Several factors could cause production interruptions, including equipment malfunctions; facility unavailability or contamination; raw material cost, shortages or contamination; natural disasters; disruption in utility services; human error; insufficient personnel; inability to meet legal or regulatory requirements; or disruptions in the operations of our suppliers.

Our product candidates will require processing steps that are more complex than those required for most small molecule drugs. Moreover, unlike small molecules, the physical and chemical properties of a complex product such as ours generally cannot be fully characterized. As a result, assays of the finished product or relevant components may not be sufficient to ensure that the product will perform in the intended manner. Accordingly, we will employ multiple steps to control the manufacturing process to assure that the process works and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims and litigation, insufficient inventory or production interruption. We may encounter problems achieving adequate quantities and quality of clinical grade materials that meet FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

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

We also may encounter problems hiring and retaining the experienced scientific, quality-control and manufacturing personnel needed to operate our manufacturing processes, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing process or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs.

We expect to rely in part on third parties to manufacture our clinical product supplies, and we intend to rely on third parties for at least a portion of the manufacturing process of our product candidates, if approved. Our business could be harmed if the third parties fail to provide us with sufficient quantities of product inputs or fail to do so at acceptable quality levels or prices or fail to meet legal and regulatory requirements.

We do not currently own any facility that may be used as our clinical-scale manufacturing and processing facility and must eventually rely on outside vendors to manufacture supplies and process our product candidates. We have not yet caused any product candidates to be manufactured or processed on a commercial scale and may not be able to do so for any of our product candidates. We will make changes as we work to optimize the manufacturing process, and we cannot be sure that even minor changes in the process will result in therapies that are safe, potent or effective.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA or other foreign regulatory agencies pursuant to inspections that will be conducted after we submit an application to the FDA or other foreign regulatory agencies. We will be dependent on our contract manufacturing partners for compliance with legal and regulatory requirements for manufacture, including cGMP, and in certain cases, cGTP, requirements of our product candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

We will rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with legal and regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential product candidates.

We will depend upon third parties, including independent investigators, to conduct our clinical trials under agreements with universities, medical institutions, CROs, strategic partners and others. We expect to have to negotiate budgets and contracts with CROs and trial sites, which may result in delays to our development timelines and increased costs.

We will rely heavily on third parties over the course of our clinical trials, and, as a result, will have limited control over the clinical investigators and limited visibility into their day-to-day activities, including with respect to their compliance with the approved clinical protocol and other legal, regulatory and scientific standards. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our legal responsibilities. We and these third parties are required to comply with good clinical practice, or GCP, requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these trials or perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP requirements. In addition, our clinical trials must be conducted with product produced under cGMP, and in certain cases, cGTP, requirements and may require a large number of test patients.

Our failure or any failure by these third parties to comply with these requirements or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates applicable federal, state or local, as well as foreign, laws and regulations, such as the fraud and abuse or false claims laws and regulations or privacy and security laws.

Any third parties conducting our future clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third parties, we cannot control whether they devote sufficient time and resources to our ongoing preclinical, clinical, and nonclinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, the transition to a new CRO may result in delays, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

Unfavorable global economic conditions or political developments could adversely affect our business, financial condition or results of operations.

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

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, theft, vandalism, accidental or intentional errors, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure or accident and are not aware of any security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our discovery and development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

Risks Related to Government Regulation

The regulatory approval process for our potential product candidates in the U.S., EU and other jurisdictions is currently uncertain and will be lengthy, time-consuming and inherently unpredictable and we may experience significant delays in the clinical development and regulatory approval, if any, of our product candidates.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products, including biologics, are subject to extensive regulation by the FDA in the U.S. and other regulatory authorities. We are not permitted to market any drug or biological product in the U.S. until we receive regulatory approval from the FDA. We have not previously submitted an NDA or BLA to the FDA, or similar approval filings to comparable foreign authorities. An NDA or BLA must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe and effective or, for biological products, safe, pure and potent for each desired indication. The application must also include significant information regarding the chemistry, manufacturing and controls for the product, and the manufacturing facilities must complete a successful pre-approval inspection by the FDA, or applicable foreign authority, prior to the approval or licensure of the product. We expect the novel nature of our product candidates to create further challenges in obtaining regulatory approval. For example, the FDA has not approved any nuclease edited cell therapies for *in vivo* or *ex vivo* human therapeutic use. The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain approval of any product candidates that we develop based on the completed clinical trials. Moreover, while we are not aware of any specific genetic or biomarker diagnostic tests for which regulatory approval would be necessary in order to advance any of our product candidates to clinical trials or potential commercialization, in the future regulatory agencies may require the development and approval of such tests. Accordingly, the regulatory approval pathway for such product candidates may be uncertain, complex, expensive and lengthy, and approval may not be obtained.

In addition, clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

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

Patient enrollment is a significant factor in the timing of clinical trials and is affected by many factors. Further, a clinical trial may be suspended or terminated by us, the IRBs for the institutions in which such trials are being conducted, the DSMB for such trial or the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience termination of, or delays in the completion of, any clinical trial of product candidates,

the commercial prospects for our product candidates will be harmed, and our ability to generate product revenue will be impaired. In addition, any delays in completing any clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and sale of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the U.S., including additional preclinical studies or clinical trials as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the U.S., a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we are allowed to charge for our products is also subject to approval.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets or to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Even if we receive regulatory approval of any product candidates or therapies, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

If any of our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, distribution, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, potency, efficacy and other post-market information, including both federal and state requirements in the U.S. and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMP and GCP, and in certain cases, cGTP, requirements for any clinical trials that we conduct post-approval.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP and, in certain cases, cGTP requirements. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA or BLA, other marketing applications, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase IV clinical trials and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, we will have to comply with legal or regulatory requirements including submissions of safety and other post-marketing information and reports and registration.

The FDA may seek to impose consent decrees or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the U.S. market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability. The policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory and legal compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

The policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the U.S. or abroad. For example, certain policies of the current or future U.S. administration may impact our business and industry. Namely, the current administration has taken, or may take, several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking and issuance of guidance. On January 30, 2017, the U.S. president issued an executive order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. In guidance issued by the Office of Information and Regulatory Affairs within OMB on April 5, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents, and on September 8, 2017, the FDA published notices in the Federal Register soliciting broad public comment to identify regulations that could be modified in compliance with these Executive Orders. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Healthcare cost control initiatives, including healthcare legislative reform measures, may have a material adverse effect on our business and results of operations.

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In both the U.S. and certain foreign jurisdictions, there have been, and are expected to continue to be, a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In the U.S., however, significant uncertainty exists regarding the provision and financing of health care because the current administration and federal legislators have publicly declared their intention to significantly modify the current legal and regulatory framework for the health care system but details have not been agreed upon or disclosed.

Current legislation at the U.S. federal and state levels seeks to reduce healthcare costs and improve the quality of healthcare. In March 2010, the Affordable Care Act was enacted, which substantially changed the way health care is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical and biotechnology industry. The Affordable Care Act, among other things, subjects biologic products to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extends the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjects manufacturers to new annual fees and taxes for certain branded prescription drugs and biologic agents and provides incentives to programs that increase the federal government's comparative effectiveness research. At this time, the full effect that the Affordable Care Act would have on our business remains unclear. Further, significant uncertainty exists regarding the future scope and effect of the Affordable Care Act because the current administration and federal legislators have publicly declared their intention to significantly modify or repeal the legislation. We cannot predict the ultimate form or timing of any modification to, or repeal of, the Affordable Care Act or the effect that such modification or repeal would have on our business. Public announcements by the U.S. administration and members of the U.S. Congress have emphasized the administration's significant interest in pursuing prompt healthcare reform. Such reform efforts and any resulting changes to the Affordable Care Act, or related regulations and laws, could impact our ability to sell our products profitably.

Other legislative changes relevant to the health care system have been adopted in the U.S. since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013, and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012, was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals and other treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In December 2017, the U.S. president signed into law the Tax Cuts and Jobs Act ("TCJA"), which among other things, repealed the Affordable Care Act's requirement that all Americans under age 65 have health insurance or pay a financial payment. These laws may result in additional reductions in Medicare, Medicaid and other healthcare funding, or insured patients generally, which could have a material adverse effect on our future, potential customers and, accordingly, our financial operations.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. As indicated previously, significant uncertainty exists regarding the future scope and effect of current health care legislation and regulations because the current administration and federal legislators have publicly declared their intention to significantly modify or repeal the current legislative framework. We cannot predict the initiatives that may be adopted in the future, any of which could limit or modify the amounts that foreign, federal and state governments as well as private payors, including patients, will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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

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

Any denial in coverage or reduction in reimbursement from Medicare or other government programs, including state and foreign programs, may result in a similar denial or reduction in payments from private payors, which may adversely affect our future profitability.

Our employees, independent contractors, clinical investigators, CROs, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of non-compliance, fraud, misconduct or other illegal activity by our employees, independent contractors, clinical investigators, CROs, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to: comply with federal and state laws and those of other applicable jurisdictions; provide true, complete and accurate information to the FDA and other similar foreign regulatory bodies; comply with manufacturing standards; comply with federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the U.S. and similar foreign privacy or fraudulent misconduct laws; or report financial information or data accurately; or disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the U.S., our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with clinical investigators and research patients, as well as proposed and future sales, marketing and education programs. In particular, the promotion, sales and marketing of healthcare products and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, including promotion and marketing of off-label uses of our products, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, physician payment transparency laws, health information privacy and security laws and anti-corruption laws. If we are unable to comply, or have not fully complied, with such laws or their relevant foreign counterparts, we could face substantial penalties.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the U.S., our operations may be directly, or indirectly through our future, potential customers and third-party payors, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations. These laws or their relevant foreign

counterparts may impact, among other things, our proposed sales, marketing, and education programs and our relationships with healthcare providers, physicians and other parties through which we market, sell and distribute our products for which we obtain marketing approval. In addition, we may be subject to patient privacy regulation by the federal government and the states in the U.S. as well as other jurisdictions. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service, for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- federal civil and criminal false claims laws and civil monetary penalties laws, including the civil False Claims Act, which impose criminal and civil penalties on individuals or entities for, among other things, knowingly presenting, or causing to be presented to the U.S. federal government, claims for payment or approval that are false or fraudulent or knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false of fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which imposes criminal and civil liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization;
- the U.S. federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act," created under the Affordable Care Act, and their implementing regulations, which require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the Centers for Medicare and Medicaid Services, information related to payments or other transfers of value made to physicians, other healthcare providers, and teaching hospitals, as well as ownership and investment interests held by physicians, other healthcare providers, and their immediate family members;
- the Foreign Corrupt Practices Act (FCPA) and other laws which prohibit improper payments or offers of payments to foreign governments and their officials and political parties by U.S. persons and issuers as defined by the statute for the purpose of obtaining or retaining business; and
- the Federal Food, Drug and Cosmetic Act, which prohibits, among other things, the commercialization of adulterated or misbranded of drugs and medical devices and the Public Health Service Act, which prohibits, among other things, the commercialization of biological products unless a biologics license is in effect.

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply regardless of the payor.

Because of the breadth of these laws and the limited statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the Affordable Care Act, among other things, amends the intent requirement of the federal Anti-Kickback Statute and criminal healthcare fraud statutes. As a result of such amendment, a person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation. Moreover, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

The increasingly global nature of our business operations subjects us to domestic and foreign anti-bribery and anti-corruption laws and regulations, such as the FCPA. Activities conducted in jurisdictions outside of the U.S. create the risk of unauthorized payments or offers of payments that are prohibited under the FCPA or comparable laws and regulations. It is our policy to implement safeguards to discourage these practices by our employees. However, these safeguards may ultimately prove ineffective, and our employees, consultants, and agents may engage in conduct for which we might be held responsible. Violations of the FCPA may result in severe criminal or civil sanctions, and we may be subject to other liabilities, which could negatively affect our business, operating results and financial condition.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations as well as other domestic and foreign legal requirements will involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other U.S. federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the U.S. will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

If we fail to comply with environmental, health and safety, and laboratory animal welfare laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous federal, state and local environmental, health and safety, and laboratory animal welfare laws and regulations. These legal requirements include those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes as well as those which regulate the care and use of animals in research. Our operations will involve research using research animals and the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also may produce hazardous waste products. We generally anticipate contracting with third parties for the disposal of these materials and wastes. We will not be able to eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from any use by us of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety, and laboratory animal welfare laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Our Intellectual Property

Third-party claims of intellectual property infringement against us, our licensors or our collaborators may prevent or delay our product discovery and development efforts.

Our commercial success depends in part on our avoiding infringement of the valid patents and proprietary rights of third parties.

Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are developing our product candidates. As industry, government, academia and other biotechnology and pharmaceutical research expands and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. We cannot guarantee that our technology, future product candidates or the use of such product candidates do not infringe third-party patents. It is also possible that we have failed to identify relevant third-party patents or applications. Because patent rights are granted jurisdiction-by-jurisdiction, our freedom to practice certain technologies, including our ability to research, develop and commercialize our product candidates, may differ by country.

Third parties may assert that we infringe their patents or that we are otherwise employing their proprietary technology without authorization, and may sue us. There may be third-party patents of which we are currently unaware with claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover product candidates we discover and develop. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies or the manufacture, use or sale of our product candidates infringes upon these patents. If any such third-party patents were held by a court of competent jurisdiction to cover our technologies or product candidates, the holders of any such patents may be able to block our ability to commercialize the applicable product candidate unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be held invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business.

Third parties may seek to claim intellectual property rights that encompass or overlap with intellectual property that we own or license from others. Legal proceedings may be initiated to determine the scope and ownership of these rights, and could result in our loss of rights, including injunctions or other equitable relief that could effectively block our ability to further develop and commercialize our product candidates. For example, through our 2014 license agreement with Caribou, we sublicense the rights of the Regents of the University of California and the University of Vienna (collectively, UC/Vienna) to a worldwide patent portfolio that covers methods of use and compositions relating to engineered CRISPR/Cas9 systems for, among other things, cleaving or editing DNA and altering gene product expression in various organisms, including eukaryotic cells. We sublicense the UC/Vienna rights to this portfolio for human therapeutic, prophylactic and palliative uses, including companion diagnostics, except for anti-fungal and anti-microbial uses. This patent portfolio to-date includes, for example, granted patents from the European Patent Office, the United Kingdom's Intellectual Property Office, the German Patent and Trade Mark Office, Australia's Intellectual Property agency and China's Intellectual Property Office. Because UC/Vienna co-own this portfolio with Dr. Emmanuelle Charpentier (from whom we do not have sublicense rights), we refer to this co-owned worldwide patent portfolio as the UC/Vienna/Charpentier patent family. The Broad Institute, Massachusetts Institute of Technology, the President and Fellows of Harvard College and the Rockefeller University co-own patents and patent applications that also claim certain aspects of CRISPR/Cas9 systems to edit genes in eukaryotic cells, including human cells (collectively, the Broad Institute patent family). Because the respective owners of a UC/Vienna/Charpentier patent application and the Broad Institute patent family both allege owning intellectual property claiming overlapping aspects of CRISPR/Cas9 systems and methods to edit genes in eukaryotic cells, including human cells, our ability to market and sell CRISPR/Cas9-based human therapeutics may be adversely impacted depending on the scope and actual ownership over the inventions claimed in the competing patent portfolios. In January 2016, an interference proceeding was declared in the U.S. Patent and Trademark Office (USPTO) between the claims from one UC/Vienna/Charpentier patent application we sublicense through Caribou and certain U.S. patents and one application of the Broad Institute patent family to determine which set of inventors invented first and, thus, is entitled to patents on the invention in the U.S. In February 2017, the PTAB dismissed the interference proceeding finding that the respective patent claims involved in the interference were distinct such that

they did not meet the legal requirement to proceed with the interference. The PTAB did not make any decision regarding inventorship or priority, and therefore ownership, of the inventions claimed by the patents and applications at issue. UC/Vienna/Charpentier appealed to the U.S. Court of Appeals for the Federal Circuit seeking a review and reversal of the PTAB's decision to terminate the interference, and the parties are waiting for a hearing and decision on the appeal. In addition, several other parties also claim and are seeking intellectual property rights that could overlap with aspects of the CRISPR/Cas9 inventions covered by the UC/Vienna/Charpentier patent portfolio, and which could result in other legal proceedings, including interference proceedings, to determine the ownership and scope of the inventions claimed by each party including UC/Vienna/Charpentier. If UC/Vienna/Charpentier are unable to prevail in their inventorship claims or if the scope of their claims is narrowed through these legal proceedings, then we could be prevented from developing and commercializing all or some of our products candidates unless we can obtain rights to the third-parties' intellectual property, or avoid or invalidate it.

Third parties could also assert patent rights against us to seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize product candidates. For example, the Broad Institute or other third-parties that own issued patents, including patents claiming aspects of the CRISPR-Cas9 technology, could seek to assert such patents against us claiming that our activities, including those relating to the CRISPR-Cas9 technology, infringe their respective patents. Defense of these or similar claims, regardless of their merit, would involve substantial legal expense, would be a substantial diversion of management and other employee resources from our business and may impact our reputation. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for any adjudicated willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. In that event, we may be unable to further develop and commercialize our product candidates, which could harm our business significantly.

Third parties asserting their patent rights against us may seek and obtain injunctive or other equitable relief, which could effectively limit or block our ability to further develop and commercialize our product candidates. If we are found to infringe a third party's valid intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing, manufacturing or importing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing one or more of our product candidates, force us to redesign our infringing products or force us to cease some or all of our business operations, any of which could materially harm our business and could prevent us from further developing and commercializing our proposed future product candidates thereby causing us significant harm. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

Intellectual property owned by third parties relating to CRISPR/Cas9 or other related technologies necessary to develop, manufacture and commercialize viable CRISPR/Cas9 therapeutics – such as compositions of the products or components, methods of treatment, delivery technologies, chemical modifications, and analytical and manufacturing methods – could adversely impact our ability to ultimately market and sell products. Third parties may own intellectual property, including patents, that cover our all or aspects of our technologies and potential products, and may be necessary for us to develop or commercialize viable products. If we are unable to successfully license, avoid or challenge such third-party intellectual property, we may not be able to develop and commercialize viable products in all or certain jurisdictions. In addition, if the intellectual property covering our products or technologies that we own or license were to be legally impaired or lost, we may be unable to realize sufficient financial returns to support the development or commercialization of our products. For additional information regarding the risks that may apply to our and our licensors' intellectual property rights, see the section entitled "Risks Related to Our Intellectual Property" appearing elsewhere in this report for more information.

Under our license agreement with Caribou, we sublicense a patent family from The Regents of the University of California and the University of Vienna that is co-owned by Dr. Emmanuel Charpentier. The outcome of recent proceedings, as well as potential future proceedings, related to this patent family may affect our ability to utilize the intellectual property sublicensed under our license agreement with Caribou.

The Broad Institute patent family includes issued patents in the U.S. and Europe that purport to cover certain aspects of the CRISPR/Cas9 gene editing platform for use on eukaryotic cells, including human cells. On January 11, 2016, the PTAB declared an interference proceeding between certain patents and a patent application of the Broad Institute patent family and one UC/Vienna/Charpentier patent application to determine, based on priority of invention, whether the contested inventions belong either to UC/Vienna/Charpentier or to the Broad Institute in the U.S. This interference proceeding was discontinued by the PTAB in February 2017 without any finding regarding inventorship or priority. In discontinuing the interference proceeding, the PTAB found that the claim sets presented by the two parties were "patentably distinct" from each other and, thus, did not meet the statutory requirements for continuing the proceeding. In April 2017, UC/Vienna/Charpentier appealed to the U.S. Court of Appeals for the Federal Circuit seeking a review and reversal of the PTAB's decision to terminate the interference, and briefing by the parties has been completed. Unless otherwise resolved, the Federal Circuit is expected to render a decision after an oral hearing. In addition, UC/Vienna/Charpentier continue to prosecute other patent claims covering the CRISPR/Cas9 inventions, which could also result in allowable or issued patents in the U.S. Certain of the claims being prosecuted by UC/Vienna/Charpentier, if found allowable by the USPTO, could lead to interference proceedings against patents or patent applications owned by other parties, including the Broad Institute patent family, with respect to certain claims expressly relating to the use of CRISPR/Cas9 in eukaryotic cells. We cannot be certain which of these results, if any, will actually occur. Further, the effects that any such results may have on us and our intellectual property position, including whether UC/Vienna/Charpentier will ultimately be successful in prosecuting to issuance a patent covering the CRISPR/Cas9 system that we are able to use under our license agreement with Caribou, are currently unknown. The Broad could seek to assert its issued patents against us based on our CRISPR/Cas9-based activities, including commercialization. Defense of these claims, regardless of their merit, would involve substantial litigation expense, would be a substantial diversion of management and other employee resources from our business and may impact our reputation. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. In that event, we could be unable to further develop and commercialize our product candidates, which could harm our business significantly.

In addition, other third parties, such as Vilnius University, ToolGene, Inc., MilliporeSigma (a subsidiary of Merck KGaA) and Harvard University, filed patent applications claiming CRISPR/Cas9-related inventions around or within a year after the UC/Vienna/Charpentier application was filed and may allege that they invented one or more of the inventions claimed by UC/Vienna/Charpentier before UC/Vienna/Charpentier. If the USPTO deems the scope of the claims of one or more of these parties to sufficiently overlap with the allowable claims from the UC/Vienna/Charpentier application, the USPTO could declare other interference proceedings to determine the actual inventor of such claims. In addition, UC/Vienna/Charpentier or the other third parties could seek judicial review of their inventorship claims. If UC/Vienna/Charpentier fail in defending their inventorship priority on any of these claims, we may lose valuable intellectual property rights, such as the exclusive right to use, such intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, any disputes could result in substantial costs and be a distraction to management and other employees.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may in the future be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor or other claims challenging the inventorship of our patents or ownership of our intellectual property (including patents and intellectual property that we in-license). For example, the UC/Vienna/Charpentier patent family that is covered by our license agreement with Caribou is co-owned by UC/Vienna and Dr. Charpentier, and our sublicense rights are derived from the first two co-owners and not from Dr. Charpentier. Therefore, our rights to these patents are not exclusive and third parties, including competitors, may have access to intellectual property that is important to our business. In addition, we may have inventorship disputes arise from conflicting obligations of collaborators, consultants or others who are

involved in developing our technology and product candidates. Litigation or other legal proceedings may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We depend on intellectual property licensed from third parties and termination or modification of any of these licenses could result in the loss of significant rights, which would harm our business.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others, including Caribou and Novartis. Any termination of these licenses, loss by our licensors of the rights they receive from others, or a finding that such intellectual property lacks legal effect, could result in the loss of significant rights and could harm our ability to commercialize any product candidates.

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

- the scope of rights, if any, granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology, products and processes infringe on, or derive from, intellectual property of the licensor that is not subject to the license agreement;
- whether our licensor or its licensor had the right to grant the license agreement, or whether they are compliant with their contractual obligations to their respective licensor(s);
- whether third parties are entitled to compensation or equitable relief, such as an injunction, for our use of the intellectual property without their authorization;
- our right to sublicense patent and other rights to third parties, including those under collaborative development relationships;
- whether we are complying with our obligations with respect to the use of the licensed technology in relation to our development and commercialization of product candidates;
- our involvement in the prosecution, defense and enforcement of the licensed patents and our licensors' overall patent strategy;
- the allocation of ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and by us and our partners; and
- the amounts of royalties, milestones or other payments due under the license agreement.

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

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

Patents relating to our product candidates are controlled by certain of our licensors or their respective licensors. Each of our licensors or their licensors generally has rights to file, prosecute, maintain and defend the patents we have licensed from such licensor. If these licensors or any future licensees and in some cases, co-owners from which we do not yet have licenses, having rights to file, prosecute, maintain, and defend our patent rights fail to adequately conduct these activities for patents or patent applications covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent

competitors from making, using or selling competing products. We cannot be certain that such activities by our licensors or their respective licensors have been or will be conducted in compliance with applicable laws and regulations or in our best interests, or will result in valid and enforceable patents or other intellectual property rights. Pursuant to the terms of the license agreements with our licensors, the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and, even if we are permitted to pursue such enforcement or defense, we cannot ensure the cooperation of our licensors or, in some cases, other necessary parties, such as the co-owners of the intellectual property from which we have not yet obtained a license. We cannot be certain that our licensors or their licensors, and in some cases, their respective co-owners, will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. For example, with respect to our sublicensed rights from Caribou to UC/Vienna/Charpentier intellectual property, UC retained the right to control the prosecution, enforcement and defense of this intellectual property in its license agreement with Caribou and, pursuant to an Invention Management Agreement, shares these responsibilities with CRISPR Therapeutics and, under certain circumstances, ERS, as the designated managers of the intellectual property. For these reasons, UC may be unable or unwilling to prosecute certain patent claims that would be best for our product candidates, or enforce its patent rights against infringers of the UC/Vienna/Charpentier patent family.

Even if we are not a party to legal actions or other disputes involving our licensed intellectual property, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. In addition, even when we have the right to control patent prosecution of licensed patents and patent applications, enforcement of licensed patents, or defense of claims asserting the invalidity of those patents, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to or after our assuming control.

We may not be successful in obtaining or maintaining necessary rights to product components and processes or other technology for our product development pipeline.

The growth of our business will likely depend in part on our ability to acquire or in-license additional proprietary rights. For example, our programs may involve additional product candidates, delivery systems or technologies that may require the use of additional proprietary rights held by third parties. Our ultimate product candidates may also require specific modifications or formulations to work effectively and efficiently. These modifications or formulations may be covered by intellectual property rights held by others. We may be unable to acquire or in-license any relevant third-party intellectual property rights that we identify as necessary or important to our business operations.

Additionally, we sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

The licensing and acquisition of third-party intellectual property rights is a competitive practice and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

If we are unable to successfully obtain rights to valid third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products or product candidates, or asserting and defending our intellectual property rights that protect our products and technologies.

We anticipate that we will file additional patent applications both in the U.S. and in other countries, as appropriate. However, we cannot predict:

- if and when any patents will issue;
- the scope, degree and range of protection any issued patents will afford us against competitors, including whether third parties will find ways to invalidate or otherwise circumvent our patents;
- whether others will apply for or obtain patents claiming aspects similar to those covered by our patents and patent applications;
- whether certain governments will appropriate our intellectual property rights and allow competitors to use them; or
- whether we will need to initiate litigation or administrative proceedings to assert or defend our patent rights, which may be costly whether we win or lose.

Composition of matter patents for biological and pharmaceutical products are generally considered to be the strongest form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of use. We cannot be certain, however, that any claims in our pending or future patent applications covering the composition of matter of our product candidates will be considered patentable by the USPTO or by patent offices in foreign countries, or that the claims in any of our ultimately issued patents will be considered valid and enforceable by courts in the U.S. or foreign countries. Method of use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label" for those uses that are covered by our method of use patents. Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The strength of patents in the biotechnology and pharmaceutical field can be uncertain, and evaluating the scope of such patents involves complex legal and scientific analyses. The patent applications that we own or in-license may fail to result in issued patents with claims that cover any product candidates or uses thereof in the U.S. or in other foreign countries.

Further, the patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner, or in all jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. We may also require the cooperation of our licensors or other necessary parties, such as the co-owners of the intellectual property from which we have not yet obtained a license, in order to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. and we may fail to seek or obtain patent protection in all major markets. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we will be unable to know with certainty whether we were the first to make any inventions claimed in any patents or patent applications, or that we were the first to file for patent protection of such inventions, nor can we know whether those from whom we license patents were the first to make the inventions claimed or were the first to file.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the U.S. and abroad. There is a substantial amount of litigation as well as administrative proceedings for challenging patents, including interference, derivation, and reexamination proceedings before the USPTO and oppositions and other comparable proceedings in foreign jurisdictions, involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, and we expect this to be true for the CRISPR/Cas9 space as well. For example, a number of third parties have filed oppositions challenging the validity, and seeking the revocation, of the CRISPR/Cas9 genome editing patent granted to UC/Vienna/Charpentier by the European Patent Office on May 10, 2017.

In addition, since the passage of the America Invents Act in 2013, U.S. law also provides for other procedures to challenge patents, including *inter partes* reviews and post-grant reviews, that add uncertainty to the possibility of challenge to our developed or licensed patents and patent applications in the future. Furthermore, for U.S. applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. See above ***Third-party claims of intellectual property infringement against us, our licensors or our collaborators may prevent or delay our product discovery and development efforts.***

Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to practice the invention or stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing their products to avoid being covered by our claims. If the breadth or strength of protection provided by the patent applications we hold is threatened, this could dissuade companies from collaborating with us to develop, and could threaten our ability to commercialize, product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market product candidates under patent protection would be reduced. Because patent applications in the U.S. and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates.

Our pending and future patent applications or the patent applications that we obtain rights to through in-licensing arrangements may not result in patents being issued which protect our technology or future product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Litigation or other administrative proceedings challenging our intellectual property, including interferences, derivation, reexamination, *inter partes* reviews and post-grant reviews, may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. Furthermore, there could be public announcement of the results of hearings, motions or other interim proceedings or developments in any proceeding challenging the issuance, scope, validity and enforceability of our developed or licensed intellectual property. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Any of these potential negative developments could impact the scope, validity, enforceability or commercial value of our patent rights and, as a result, have material adverse effect on our business, financial condition, results of operations or prospects.

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

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent. We also utilize proprietary processes for which patents are difficult to enforce. In addition, other elements of our product discovery and development processes involve proprietary know-how, information, or technology that is not covered by patents. Trade secrets, however, may be difficult to protect. We seek to protect our proprietary processes, in part, by entering into confidentiality agreements with our employees, consultants, outside scientific advisors, contractors, and collaborators. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, outside scientific advisors, contractors, and collaborators might intentionally or inadvertently disclose our trade secret information to competitors. In addition, competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the U.S. and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, or misappropriation of our intellectual property by third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results, and financial condition.

We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world.

We have limited intellectual property rights outside the U.S. Filing, prosecuting, maintaining and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. can have a different scope and strength than do those in the U.S. In addition, the laws of some foreign countries, such as China, Brazil, Russia, India, and South Africa, do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as those in the U.S. These products may compete with our products and our patents or other intellectual property rights may not be effective or adequate to prevent them from competing. In addition, in jurisdictions outside the U.S., a license may not be enforceable unless all the owners of the intellectual property agree or consent to the license. Further, patients may choose to travel to countries in which we do not have intellectual property rights or which do not enforce these rights to obtain the products or treatment from competitors in such countries.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, such as China, Brazil, Russia, India, and South Africa, do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to biopharmaceutical products, which could make it difficult in those jurisdictions for us to stop the infringement or misappropriation of our patents or other intellectual property rights, or the marketing of competing products in violation of our proprietary rights. Proceedings to enforce our patent and other intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, such proceedings could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims of infringement or misappropriation against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming, and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To cease such infringement or unauthorized use, we may be required to file patent infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding or a declaratory judgment action against us, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology

at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

Interference or derivation proceedings provoked by third parties or brought by the USPTO may be necessary to determine the priority of inventions with respect to, or the correct inventorship of, our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Litigation, interference or derivation proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or proceeding. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or before the USPTO or comparable foreign authority.

If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the U.S. or other jurisdictions, even outside the context of litigation. Such mechanisms include re-examination, *inter partes* review, post-grant review and equivalent proceedings in foreign jurisdictions, such as opposition or derivation proceedings. Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity, unpatentability and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies as well as academic research institutions. We may be subject to claims that we or our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees' former employers. Litigation may be necessary to defend against these claims, which could result in money damages or judicial order prohibiting the use of certain intellectual property. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

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

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent

application process. Although an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. In any such event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

We may be required to pay certain milestones and royalties under our license agreements with third-party licensors.

Under our current and future license agreements, we may be required to pay milestones and royalties based on our revenues from sales of our products utilizing the technologies licensed or sublicensed from third parties, including Caribou, Novartis and Regeneron, and these royalty payments could adversely affect the overall profitability for us of any products that we may seek to commercialize. In order to maintain our license rights under these license agreements, we will need to meet certain specified milestones, subject to certain cure provisions, in the development of our product candidates and in the raising of funding. In addition, these agreements contain diligence milestones and we may not be successful in meeting all of the milestones in the future on a timely basis or at all. We will need to outsource and rely on third parties for many aspects of the clinical development, sales and marketing of our products covered under our license agreements. Delay or failure by these third parties could adversely affect the continuation of our license agreements with their third-party licensors.

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

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or future, potential customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Risks Related to Our Common Stock

An active trading market for our common stock may not be sustained.

In May 2016, we closed our initial public offering. Prior to this offering, there was no public market for our common stock. Although we have completed our initial public offering and shares of our common stock are listed and trading on the Nasdaq Global Market, an active trading market for our shares may not be sustained. If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or sell their shares at or above the prices at which they acquired their shares or sell their shares at the time they would like to sell. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

The price of our common stock historically has been volatile, which may affect the price at which you could sell any shares of our common stock.

The market price for our common stock historically has been highly volatile and could continue to be subject to wide fluctuations in response to various factors. This volatility may affect the price at which you could sell the shares of our common stock, and the sale of substantial amounts of our common stock could adversely affect the price of our common stock. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and other factors, including:

- the success of our or competing products or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- developments or disputes concerning patent applications, issued patents or other intellectual property rights;
- regulatory or legal developments in the U.S. and other countries;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or the financial results of companies that are perceived to be similar to us;
- sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this *Risk Factors* section.

In addition, companies trading in the stock market in general, and in the Nasdaq Global Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Our principal stockholders and management own a significant percentage of our stock and, if they choose to act together, will be able to control or exercise significant influence over matters subject to stockholder approval.

As of December 31, 2017, our executive officers, directors, five percent or greater stockholders and their affiliates beneficially own approximately 54.0% of our outstanding voting stock. These stockholders may have the ability to influence us through their ownership positions. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We have broad discretion over the use of our cash and cash equivalents and may not use them effectively.

Our management has broad discretion to use our cash and cash equivalents to fund our operations and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending our use to fund operations, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of stockholders and could cause our stock price to fall.

The Company will need additional capital in the future to continue our planned operations in addition to the proceeds we received from our initial public offering in May 2016 and follow-on public offering in November 2017. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to the Company's existing stockholders, and new investors could gain rights superior to our existing stockholders.

In addition, sales of a substantial number of shares of our outstanding common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Persons who were our stockholders prior to our IPO continue to hold a substantial number of shares of our common stock that many of them are now able to sell in the public market. Significant portions of these shares are held by a relatively small number of stockholders. Sales by our stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us difficult, limit attempts by our stockholders to replace or remove our current management and adversely affect our stock price.

Provisions of our certificate of incorporation and by-laws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our stock. Among other things, the certificate of incorporation and by-laws:

- permit the board of directors to issue up to 5,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that the authorized number of directors may be changed only by resolution of the board of directors;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide the board of directors into three classes;
- provide that a director may only be removed from the board of directors by the stockholders for cause;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders, and may not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner, and meet specific requirements as to the form and content of a stockholder's notice;

- prevent cumulative voting rights (therefore allowing the holders of a plurality of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- require that, to the fullest extent permitted by law, a stockholder reimburse us for all fees, costs and expenses incurred by us in connection with a proceeding initiated by such stockholder in which such stockholder does not obtain a judgment on the merits that substantially achieves the full remedy sought;
- provide that special meetings of our stockholders may be called only by the chairman of the board, our chief executive officer (or president, in the absence of a chief executive officer) or by the board of directors; and
- provide that stockholders will be permitted to amend the bylaws only upon receiving at least two-thirds of the total votes entitled to be cast by holders of all outstanding shares then entitled to vote generally in the election of directors, voting together as a single class.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any "interested" stockholder for a period of three years following the date on which the stockholder became an "interested" stockholder.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our by-laws, any action to interpret, apply, enforce, or determine the validity of our certificate of incorporation or bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find the choice of forum provision contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

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

As a public company, and particularly after we are no longer an "emerging growth company" under applicable SEC regulations, we incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 (Section 404), we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we are not required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts may not publish an adequate amount of research on the Company, which may negatively impact the trading price for our stock. In addition, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. Further, if our operating results fail to meet the forecasts of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of the Company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

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

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

Changes in tax law may adversely affect our business and financial condition.

The laws and rules dealing with U.S. federal, state and local income and other taxation are routinely reviewed by the relevant legislative entity and regulatory agencies, such as the IRS and the U.S. Treasury Department, for federal tax rules. Changes to tax laws and rules (which changes may have retroactive application) could adversely affect us or holders of our common stock. Since the Company was founded in 2014, many such changes have been made and changes are likely to continue to occur in the future. For example, in December 2017, the U.S. president signed into law the TCJA that significantly reforms the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility or interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and effectuates the migration from a "worldwide" system of taxation to a territorial system. Our net deferred tax assets and liabilities have been revalued at the newly enacted U.S. corporate rate. The impact of this tax reform is uncertain and could be adverse. It cannot be predicted whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or issued, that could result in an increase in our or our shareholders' tax liability.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our headquarters are located at 40 Erie Street in Cambridge, Massachusetts, where we occupy approximately 65,000 square feet of office and laboratory space. This lease expires in November 2026, and we have an option to extend the term of the lease for an additional three years. In addition, we lease approximately 15,200 square feet of office and laboratory space at 130 Brookline Street in Cambridge, Massachusetts. This lease expires in January 2020, and we have an option to extend it through January 2025.

Item 3. Legal Proceedings

From time to time, we may be subject to legal proceedings and claims in the ordinary course of business. We are not currently aware of any such proceedings or claims that we believe will have, individually or in the aggregate, a material adverse effect on our business, financial condition or results of operations. On April 13, 2015, UC/Vienna/Charpentier jointly filed a request with the United States Patent and Trademarks Office (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), 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 (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 to terminate the interference, and briefing on the appeal was completed in November 2017. Unless otherwise resolved, the Federal Circuit is expected to render a decision after an oral hearing. The timing for a decision in this matter is unknown.

In addition, both UC/Vienna/Charpentier and the Broad, as well as other third parties, such as Vilnius University, ToolGen, Inc., MilliporeSigma (a subsidiary of Merck KGaA) and Harvard University, continue to prosecute other patent claims covering the CRISPR/Cas9 inventions, which could also result in allowable or issued patents in the United States and in other jurisdictions. In the United States, certain of the claims being prosecuted by UC/Vienna/Charpentier, if found allowable by the USPTO, could lead to interference proceedings against patents or patent applications owned by other parties, including the Broad Institute patent family with respect to certain claims relating to the use of CRISPR/Cas9 in eukaryotic cells, as well as other third-parties such as Vilnius University, ToolGen and Sigma-Aldrich and Harvard. Outside the United States, the Broad and ToolGen have filed international counterparts of their U.S. applications, some of which were granted in Europe and/or other jurisdictions, and Vilnius University and other third parties also have international counterparts of U.S. patent applications that could proceed to grant. We, and several other parties, have filed oppositions against some of these granted patents, and we may in the future oppose other patents granted to third parties seeking to cover aspects of the CRISPR/Cas9 technology or other technology relevant to our operations. Similarly, if UC/Vienna/Charpentier, our licensors or we should obtain patents in the U.S., Europe and other jurisdictions, third parties may file legal challenges, including re-examination, oppositions or other post-grant challenges, seeking to revoke or narrow claims in the patents. Based on the interest in CRISPR/Cas9 technology, as well as the number of current post-grant proceedings against patents covering the technology, we reasonably expect that CRISPR/Cas9 technology patents, including those owned by UC/Vienna/Charpentier, our other licensors and the Company, will be the subject of legal challenges in the United States and internationally.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for the Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our common stock is traded on the Nasdaq Global Market under the symbol "NTLA". Trading of our common stock commenced on May 6, 2016, following the completion of our initial public offering. The following table sets forth the high and low sale prices per share of our common stock, as reported on the Nasdaq Global Market, for the periods indicated:

	Market Price	
	High	Low
Year ended December 31, 2017:		
Fourth quarter	$ 33.34	$ 16.33
Third quarter	$ 26.70	$ 14.45
Second quarter	$ 17.61	$ 11.15
First quarter	$ 15.78	$ 10.83

	Market Price	
	High	Low
Year ended December 31, 2016:		
Fourth quarter	$ 19.66	$ 11.86
Third quarter	$ 24.90	$ 16.60
Second quarter (from May 6, 2016)	$ 30.40	$ 20.70

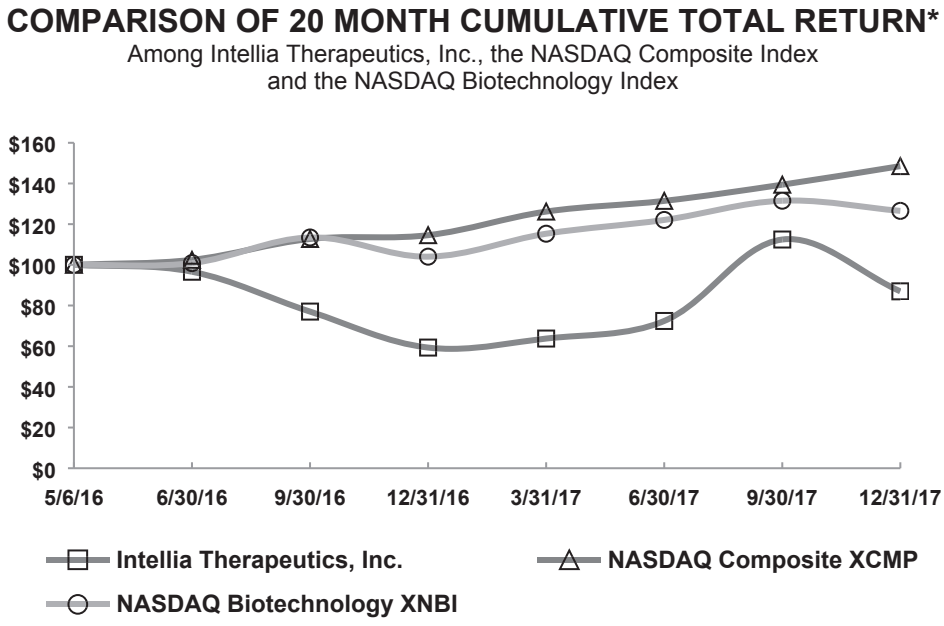
As of February 28, 2018, the number of holders of record of our common stock was 41. This number does not include beneficial owners whose shares are held in street name.

Dividends

We have never declared or paid cash dividends on our capital stock. We intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future.

Stock Performance Graph

The following graph shows a comparison from May 6, 2016, the first date that shares of our common stock were publicly traded, through December 31, 2017, of the cumulative total return on an assumed investment of $100.00 in cash in our common stock, the Nasdaq Composite Index and the Nasdaq Biotechnology Index for the same period. Such returns are based on historical results and are not intended to suggest future performance. Data for the Nasdaq Composite Index and the Nasdaq Biotechnology Index assume reinvestment of dividends.



The performance graph in this Item 5 is not deemed to be "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Securities and Exchange Act of 1934, as amended, or otherwise subject to the liabilities under that Section, and shall not be deemed incorporated by reference into any of our filings under the Securities Act of 1933 or the Securities Exchange Act of 1934, except to the extent we specifically incorporate it by reference into such a filing.

Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

Use of Proceeds from Initial Public Offering of Common Stock

In May 2016, we issued and sold 6,900,000 shares of our common stock, including 900,000 shares of common stock sold pursuant to the underwriters' full exercise of their option to purchase additional shares, in our initial public offering ("IPO") at a public offering price of $18.00 per share, for aggregate gross proceeds of $124.2 million. All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-210689), which was declared effective by the SEC on May 5, 2016. Credit Suisse

Securities (USA) LLC, Jeffries LLC and Leerink Partners LLC acted as joint book-running managers of the offering and as representatives of the underwriters. Wedbush Securities Inc. acted as manager for the offering. The offering commenced on May 5, 2016 and did not terminate until the sale of all of the shares offered.

The estimated net proceeds to us, after deducting underwriting discounts of $8.7 million and offering expenses of $3.4 million, were approximately $112.1 million. No offering expenses were paid directly or indirectly to any of our directors or officers, or their associates, or persons owning 10.0% or more of any class of our equity securities or to any other affiliates.

As of December 31, 2017 we have used all of the net proceeds, primarily to advance the research and development of our product candidates for our initial indications, to progress additional *in vivo* and *ex vivo* pipeline development candidates, to further develop our delivery technologies and CRISPR/Cas9 genome editing platform and for working capital and general corporate purposes.

Item 6. Selected Financial Data

The following selected financial data has been derived from our consolidated financial statements. The information set forth below should be read in conjunction with Item 7. *Management's Discussion and Analysis of Financial Condition and Results of Operations* and with our consolidated financial statements and notes thereto included elsewhere in this document.

We derived the consolidated financial data for the years ended December 31, 2017, 2016 and 2015 and for the period from May 7, 2014 (inception) to December 31, 2014 and as of December 31, 2017, 2016, 2015 and 2014 from our audited consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K. Historical results are not necessarily indicative of the results to be expected in future periods.

	Year Ended December 31,			Period from May 7, 2014 (inception) to December 31,
	2017	2016	2015	2014
	(in thousands except per share data)			
Consolidated Statements of Operations Data:				
Collaboration revenue	$ 26,117	$ 16,479	$ 6,044	$ -
Operating expenses:				
Research and development	67,647	31,840	11,170	1,105
In-process research and development	-	-	-	6,055
General and administrative	28,025	16,798	8,283	2,379
Total operating expenses	95,672	48,638	19,453	9,539
Operating loss	(69,555)	(32,159)	(13,409)	(9,539)
Interest income	2,012	525	-	-
Loss before income taxes	(67,543)	(31,634)	(13,409)	(9,539)
Income tax benefit	-	-	1,012	-
Net loss	$ (67,543)	$ (31,634)	$ (12,397)	$ (9,539)
Net loss per share or common unit, basic and diluted	$ (1.88)	$ (1.42)	$ (51.02)	$ (11.55)
Weighted average shares or common units outstanding, basic and diluted	36,006	22,222	243	826

	As of December 31,			
	2017	2016	2015	2014
		(in thousands)		
Consolidated Balance Sheet Data:				
Cash and cash equivalents	$340,678	$273,064	$ 75,816	$ 9,845
Working capital (1)	323,471	250,576	66,931	7,775
Total assets	376,235	298,969	82,139	10,694
Deferred revenue	65,299	78,287	10,312	-
Convertible preferred stock	-	-	88,557	-
Total stockholders' equity	300,597	209,837	(21,201)	7,566

(1) We define working capital as current assets less current liabilities.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

Our management's discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements included in this Annual Report on Form 10-K, which have been prepared by us in accordance with U.S. generally accepted accounting principles, or GAAP, 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 consolidated financial statements and the notes thereto included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in Part I, Item 1A. *Risk Factors* of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

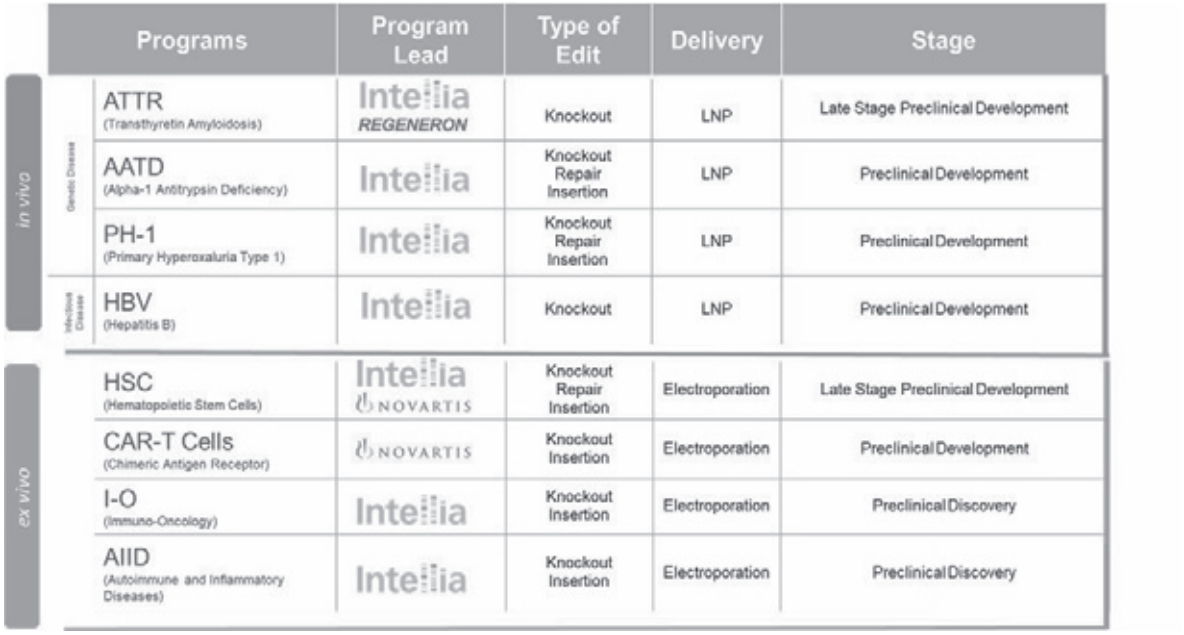
Management Overview

Intellia Therapeutics, Inc. ("we," "us," "our," "Intellia," or the "Company") is a leading genome editing 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 transform medicine by permanently editing disease-associated genes or genetic material in the human body with a single treatment course. We intend to leverage our leading scientific expertise, clinical development experience and intellectual property position to unlock broad therapeutic applications of CRISPR/Cas9 genome editing and develop a potential new class of therapeutic products.

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), our initial public offering and private placements of our common and preferred stock. All of our revenue to date has been collaboration revenue. Since our inception and through December 31, 2017, we have raised an aggregate of approximately $502.6 million to fund our operations, of which $106.1 million was through our collaboration agreements, $170.5 million was from our initial public offering and concurrent private placements, $141.0 million was from a secondary offering and $85.0 million was from the sale of convertible preferred stock.

We believe our product focus, therapeutic discovery and development strength, delivery expertise and intellectual property 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 risk-mitigating approach with our initial indications. Our approach is defined by four primary criteria: (i) the type of edit—knockout, repair or insertion; (ii) the delivery modality for *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, which we are co-developing with Regeneron, alpha-1 antitrypsin deficiency, inborn errors of metabolism, including primary hyperoxaluria, and chronic hepatitis B infection – as well as *ex vivo* applications of the technology in chimeric antigen receptor T cell (CAR-T cell) and hematopoietic stem cell (HSC), product candidates which are selectively partnered with our collaborator Novartis.

The following table illustrates our discovery programs and opportunities as of February 28, 2018:



		Programs	Program Lead	Type of Edit	Delivery	Stage
in vivo	Genetic Disease	ATTR (Transthyretin Amyloidosis)	Intellia / REGENERON	Knockout	LNP	Late Stage Preclinical Development
		AATD (Alpha-1 Antitrypsin Deficiency)	Intellia	Knockout Repair Insertion	LNP	Preclinical Development
		PH-1 (Primary Hyperoxaluria Type 1)	Intellia	Knockout Repair Insertion	LNP	Preclinical Development
	Infectious Disease	HBV (Hepatitis B)	Intellia	Knockout	LNP	Preclinical Development
ex vivo		HSC (Hematopoietic Stem Cells)	Intellia / NOVARTIS	Knockout Repair Insertion	Electroporation	Late Stage Preclinical Development
		CAR-T Cells (Chimeric Antigen Receptor)	NOVARTIS	Knockout Insertion	Electroporation	Preclinical Development
		I-O (Immuno-Oncology)	Intellia	Knockout Insertion	Electroporation	Preclinical Discovery
		AIID (Autoimmune and Inflammatory Diseases)	Intellia	Knockout Insertion	Electroporation	Preclinical Discovery

In September 2017, we presented data from our completed long-term, 52-week, durability mouse study, demonstrating *in vivo* genome editing following a single, intravenous administration of CRISPR/Cas9. With a single dose, we achieved and maintained an approximately 97 percent reduction in serum TTR protein levels through 12 months. This TTR reduction was accomplished by approximately 70 percent sustained editing at the target DNA site in the liver. This study confirmed that our lipid nanoparticle (LNP) system is transiently present with 99 percent clearance of messenger RNA (mRNA) within 10 hours and of single guide RNA (sgRNA) within 72 hours in the liver. The treatment was well-tolerated at the time of administration and no adverse events were noted throughout the 52-weeks of follow-up study. These mouse durability results followed our presentation in August 2017 of initial data from rat studies demonstrating *in vivo* genome editing after a single, intravenous administration of CRISPR/Cas9. In our August 2017 presentation, we reported that, using our LNP system in rats, we had observed up to 91 percent reduction in serum TTR protein levels and up to 66 percent editing at the target DNA site in the subject animals.

In October 2017, we released interim top-line data regarding our *in vivo* non-human primate (NHP) exploratory pre-clinical studies. Specifically, based on preliminary studies currently at varying points of progress, liver genome editing rates using CRISPR/Cas9 delivered via our proprietary LNP system have ranged from 0.10 percent up to 32.0 percent after a single dose with various exploratory NHP guide RNAs (gRNA), LNP formulations and dosing regimens as well as with exploratory human cross-reactive gRNAs. In NHPs redosed with a subsequent application of our LNP formulations, we observed further editing that surpassed those levels achieved after a single dose, with multiple animals achieving a total of over 20 percent liver genome editing after a second dose.

These NHP results were similar to the results we observed in our initial rodent studies. We are conducting further optimization of our delivery system and proceeding to human guide selection. We expect to achieve higher levels of editing and reductions in serum levels of TTR protein as we achieved when we optimized the delivery system and CRISPR/Cas9 cargo used in our rodent models. We expect to begin IND-enabling activities for a human therapeutic as soon as mid-2018.

To date, in both single and repeat dose experiments, our proprietary delivery LNP system has been well-tolerated with both NHP-specific gRNA and exploratory human cross-reactive gRNAs, as assessed by gross observation of the animals, clinical chemistry, hematology, and cytokine and complement levels. We are also encouraged by the reduction in serum TTR protein levels shown to date in animals with the highest levels of editing. We are

conducting additional studies in multiple animal models to maximize editing rates through repeat dosing and formulation optimization.

In October 2017, we presented data from an *in vivo* mouse study showing, after a single systemic intracerebral injection, delivery to the brain of 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 gene 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, editing levels from less than 1% up to 28% were achieved in the striatal and cerebellar tissue. The injections were well tolerated and the mice did not display any behavioral changes post dosing.

In December 2017, our collaborator Novartis presented initial data from our research collaboration on genome-edited human hematopoietic stem cells. 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 stably engraft in mice while maintaining their desired properties. Specifically, the data showed that approximately 80-95 percent target site modification in human hematopoietic stem and progenitor CD34+ cells was achieved following electroporation of ribonucleoprotein (RNP) composed of Cas9 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 γ-globin transcript and 30-40 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 γ-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.

Collaborations

Novartis

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

Through December 31, 2017, excluding amounts allocated to Novartis' purchase of our Class A-1 and Class A-2 Preferred Units, we had recorded a total of $34.4 million in cash and accounts receivable under the Novartis agreement. Through December 31, 2017, we have recognized $23.1 million of collaboration revenue, including $9.3 million, $7.8 million and $6.0 million in the years ended December 31, 2017, 2016 and 2015, respectively, in the consolidated statements of operations related to this agreement. As of December 31, 2017 and December 31, 2016, we had accounts receivable of $6.0 million and $6.0 million, respectively, related to this agreement. As of December 31, 2017 and 2016, we had deferred revenue of $11.2 million and $11.6 million, respectively, related to this agreement.

Regeneron

As described in "Collaborations—Regeneron Pharmaceuticals, Inc.," 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.

Through December 31, 2017, we have recorded a $75.0 million upfront payment and $4.6 million for research and development services under the Regeneron agreement. Through December 31, 2017, we have recognized $25.5

million of collaboration revenue, including $16.8 million and $8.7 million in the years ended December 31, 2017 and 2016, respectively. As of December 31, 2017 and December 31, 2016, we had accounts receivable of $4.5 million and $0.5 million, respectively, related to this agreement. As of December 31, 2017 and 2016, we had deferred revenue of $54.1 million and $66.7 million, respectively, related to this agreement.

Financial Overview

Collaboration Revenue

Our revenue consists of collaboration revenue, including amounts recognized related to upfront technology access payments for licenses, technology access fees, research funding and milestone payments earned under our collaboration and license agreements with Novartis and Regeneron.

Research and Development

Research and development expenses consist of expenses incurred in performing research and development activities, including compensation and benefits, which includes equity-based compensation, for full-time research and development employees, facility-related expenses, overhead expenses, lab supplies and contract research services.

General and Administrative

General and administrative expenses consist primarily of salaries and benefits, including equity-based compensation, for our executive, finance, legal, business development and support functions. 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 intellectual property-related legal services, and other consulting fees and expenses.

Interest Income

Interest income is income earned on our cash equivalents.

Results of Operations

Comparison of Years Ended December 31, 2017, and 2016

The following table summarizes our results of operations for the years ended December 31, 2017 and 2016:

	Year Ended December 31,		Period-to-Period Change
	2017	2016	
Collaboration revenue	$ 26,117	$ 16,479	$ 9,638
Operating expenses:			
Research and development	67,647	31,840	35,807
General and administrative	28,025	16,798	11,227
Total operating expenses	95,672	48,638	47,034
Operating loss	(69,555)	(32,159)	(37,396)
Interest income	2,012	525	1,487
Loss before income taxes	(67,543)	(31,634)	(35,909)
Income tax provision	-	-	-
Net loss	$ (67,543)	$ (31,634)	$ (35,909)

Collaboration Revenue

Collaboration revenue increased $9.6 million to $26.1 million during the year ended December 31, 2017, as compared to $16.5 million during the year ended December 31, 2016. The increase in collaboration revenue during the year ended December 31, 2017 is primarily related to the recognition of amounts under the Regeneron collaboration for a full year, including increased research and development services, as well as timing of the collaborations and the related commencement of amortization of the deferred revenue balances.

During the years ended December 31, 2017 and 2016, collaboration revenue consisted of amounts recognized from deferred revenue related to upfront technology access payments for licenses, technology access fees and research funding under the Novartis collaboration as well as amounts recognized from deferred revenue related to an upfront payment received and amounts for research and development services under the Regeneron collaboration.

Research and Development

Research and development expenses increased $35.8 million to $67.6 million during the year ended December 31, 2017, as compared to $31.8 million during the year ended December 31, 2016. This increase is primarily driven by our growth to 148 research and development employees as of December 31, 2017 from 77 research and development employees as of December 31, 2016, and the further advancement of our early-stage research programs, collectively resulting in increases in salaries and related compensation expenses, facilities-related expenses as we moved into our new office space at the end of 2016 and invested in laboratory equipment through 2017, as well as laboratory supplies and research materials.

During 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 increased by $11.2 million to $28.0 million during the year ended December 31, 2017, as compared to $16.8 million during the year ended December 31, 2016. This increase is primarily related to increased salary and related headcount-based expenses, including equity-based compensation expense, as we grew to 36 general and administrative employees as of December 31, 2017 from 27 general and administrative employees as of December 31, 2016, as well as increased facilities-related expenses as we moved into our new office space at the end of 2016.

Interest Income

Interest income increased by $1.5 million to $2.0 million during the year ended December 31, 2017 as compared to $0.5 million during the year ended December 31, 2016. This increase was caused by an increase in our average cash balance year over year.

Comparison of Years Ended December 31, 2016, and 2015

The following table summarizes our results of operations for the years ended December 31, 2016 and 2015:

	Year Ended December 31,		Period-to-Period Change
	2016	2015	
Collaboration revenue	$ 16,479	$ 6,044	$ 10,435
Operating expenses:			
Research and development	31,840	11,170	20,670
General and administrative	16,798	8,283	8,515
Total operating expenses	48,638	19,453	29,185
Operating loss	(32,159)	(13,409)	(18,750)
Interest income	525	-	525
Loss before income taxes	(31,634)	(13,409)	(18,225)
Income tax benefit	-	1,012	(1,012)
Net loss	$ (31,634)	$ (12,397)	$ (19,237)

Collaboration Revenue

Collaboration revenue increased $10.4 million to $16.5 million during the year ended December 31, 2016, as compared to $6.0 million during the year ended December 31, 2015. The increase in collaboration revenue during the year ended December 31, 2016 is related to the recognition of amounts under the Regeneron collaboration, which was entered into in April 2016.

During the year ended December 31, 2016, collaboration revenue consisted of amounts recognized from deferred revenue related to upfront technology access payments for licenses, technology access fees and research funding under the Novartis collaboration as well as amounts recognized from deferred revenue related to an upfront payment received and amounts for research and development services under the Regeneron collaboration. During the year ended December 31, 2015, collaboration revenue consisted of amounts recognized from deferred revenue related to upfront technology access payments for licenses, technology access fees and research funding under the Novartis collaboration.

Research and Development

Research and development expenses increased $20.6 million to $31.8 million during the year ended December 31, 2016, as compared to $11.2 million during the year ended December 31, 2015. This increase is primarily driven by our growth to 77 research and development employees as of December 31, 2016 from 38 research and development employees as of December 31, 2015, and the advancement of our early-stage research programs, collectively resulting in increases in salaries and related compensation expenses as well as laboratory supplies and research materials and services.

General and Administrative

General and administrative expenses increased by $8.5 million to $16.8 million during the year ended December 31, 2016, as compared to $8.3 million during the year ended December 31, 2015. This increase is primarily related to increased salary and related headcount-based expenses, including equity-based compensation expense, as we grew to 27 general and administrative employees as of December 31, 2016 from 14 general and administrative employees as of December 31, 2015, as well as increased corporate insurance, legal and other professional expenses related to our operations as a public company beginning in May 2016.

Interest Income

Interest income increased by $0.5 million during the year ended December 31, 2016 as compared to the same period in 2015. This increase is due to the inclusion of interest-bearing money market accounts, commercial paper and U.S. treasury securities throughout 2016, as compared to no interest-bearing instruments in the prior year.

Income Tax Expense

We did not recognize any net benefit from income taxes during the year ended December 31, 2017 or 2016 due to our uncertainty of realizing a tax benefit from the deferred tax assets. During the year ended December 31, 2015, we allocated $2.6 million from the $30.0 million total fixed amount of consideration under the collaboration agreement with Novartis to the carrying value of the Class A-1 and Class A-2 preferred units to record those units based on their fair value at date of issuance. As a result of this allocation, during the year ended December 31, 2015, we recorded an income tax provision of $1.0 million within members' equity as well as a corresponding income tax benefit of $1.0 million within continuing operations.

Liquidity and Capital Resources

Since our inception through December 31, 2017, we have raised an aggregate of $502.6 million to fund our operations, of which $106.1 million was through our collaboration agreements, $170.5 million was from our initial public offering and concurrent private placements, $141.0 million was from a secondary offering in 2017 and $85.0 million was from the sale of convertible preferred stock. As of December 31, 2017, we had $340.7 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.

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 intellectual property and general overhead costs. During 2018, 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 December 31, 2017, 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 intellectual property 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 years ended December 31, 2017, 2016 and 2015:

	Year Ended December 31,		
	2017	2016	2015
	(In millions)		
Net cash (used in) provided by operating activities	$ (65.3)	$ 36.1	$ (1.8)
Net cash used in investing activities	(10.1)	(6.2)	(2.6)
Net cash provided by financing activities	143.0	167.3	70.3

Net cash (used in) provided by operating activities

Net cash used in operating activities of $65.3 million during the year ended December 31, 2017 primarily reflects increased spend in our research and development and general and administrative activities, offset in part by the receipt of $9.0 million in additional payments from Novartis. Net cash provided by operating activities of $36.1 million during the year ended December 31, 2016 primarily reflects the receipt of a $75.0 million upfront payment under our collaboration with Regeneron and $4.0 million in additional payments from Novartis, offset in part by spend in our research and development and general and administrative activities as well as the payment of a $2.2 million security deposit for our new office and laboratory facilities in Cambridge, Massachusetts. Net cash used in operating activities of $1.8 million in the year ended December 31, 2015 primarily reflected compensation, laboratory and professional service expenses, offset in part by the receipt of a $10.0 million upfront technology access payment and $5.0 million annual technology access fee under the Novartis collaboration agreement, net of $2.6 million of such payments which was allocated to the recording of preferred units acquired by Novartis.

Net cash used in investing activities

Net cash used in investing activities during the years ended December 31, 2017, 2016 and 2015 relate to purchases of property and equipment as we grow our operations and build out our office and laboratory facilities.

Net cash provided by financing activities

Net cash provided by financing activities of $143.0 million during the year ended December 31, 2017 includes $141.0 million in proceeds from our secondary offering, $1.2 million in cash received from the exercise of stock options and $0.8 million in cash received from the issuance of shares through our employee stock purchase plan. Net cash provided by financing activities of $167.3 million during the year ended December 31, 2016 includes $170.5 million in proceeds from our initial public offering and concurrent private placements, offset in part by the payment of offering costs and amounts paid that were allocated to the value of the intellectual property licensed from Caribou. Net cash provided by financing activities during the year ended December 31, 2015 related to the sale of preferred securities for net proceeds of $2.0 million, receipt of $2.6 million in consideration from Novartis related to

their purchase of preferred securities from us and completion of the sale of preferred securities to new and existing investors for aggregate net proceeds of $67.4 million.

Contractual Obligations

The following summarizes our contractual obligations as of December 31, 2017:

	Payments Due by Period				
	Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
			(In millions)		
Property leases	$ 25.4	$ 5.5	$ 10.6	$ 9.3	$ -

The amounts reported for property leases represent future minimum lease payments under non-cancelable operating leases in effect as of December 31, 2017. The minimum lease payments do not include common area maintenance charges or real estate taxes.

The contractual obligations table does not include any potential future pass-through milestone payments of up to $26.4 million or royalty payments we may be required to make under the Caribou license agreement, through which we have received rights to CRISPR/Cas9 intellectual property for a specified field of human therapeutic applications, due to the uncertainty of the occurrence of the events requiring payment under that agreement. The table also excludes our obligation to pay 30.0% of Caribou's patent prosecution filing and maintenance costs for licensed intellectual property as such costs cannot be reliably estimated until incurred.

Under the Caribou license agreement, we sublicense a patent family that has been subject to interference proceedings declared by the Patent Trial and Appeal Board (PTAB) of the United States Patent and Trademarks Office (USPTO). Although these interference proceedings were dismissed by the PTAB on February 15, 2017, additional substantial legal expenses may be incurred in relation to any appeal of the PTAB decision or any continued prosecution of other claims from the patent family or potential additional interference proceedings. In addition, the parties opposing the interference may seek to assert their intellectual property against us based on our scientific or business activities, including during commercialization. Defense of any such claims would involve substantial litigation expense, and any successful claim of infringement against us could require us to pay substantial damages or result in an injunction against one or more of our products.

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of financial condition and results of operations is based upon our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S. The preparation of these consolidated financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities as of the date of the balance sheets and the reported amounts of collaboration revenue and expenses during the reporting periods. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances at the time such estimates are made. Actual results and outcomes may differ materially from our estimates, judgments and assumptions. We periodically review our estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates are reflected in the consolidated financial statements prospectively from the date of the change in estimate.

We define our critical accounting policies as those accounting principles generally accepted in the U.S. that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations as well as the specific manner in which we apply those principles. We believe the critical accounting policies used in the preparation of our consolidated financial statements which require significant estimates and judgments are as follows:

Revenue Recognition

We recognize revenue for each identified unit of accounting when all of the following criteria are met: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the seller's price to the buyer is fixed or determinable; and collectability is reasonably assured.

The terms of our collaboration and license agreements contain multiple deliverables, which include licenses to CRISPR/Cas9-based therapeutic products directed to specific targets, referred to as exclusive licenses, as well as research and development activities to be performed by us on behalf of the collaboration partner related to the licensed targets. Payments that we may receive under these agreements include non-refundable technology access fees, payments for research activities, payments based upon the achievement of specified milestones and royalties on any resulting net product sales.

Multiple-Element Arrangements

Our collaboration and license agreements represent multiple-element arrangements. We evaluate our collaborative agreements for proper classification in our statements of operations based on the nature of the underlying activity. We generally reflect as revenue amounts due under our collaborative agreements related to reimbursement of development activities as we are generally the principal under the arrangement.

We evaluate multiple-element arrangements to determine (i) the deliverables included in the arrangement and (ii) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. When deliverables are separable, consideration received is allocated to the separate units of accounting based on the relative selling price method and the appropriate revenue recognition principles are applied to each unit. When we determine that an arrangement should be accounted for as a single unit of accounting, we must determine the period over which the performance obligations will be satisfied and revenue will be recognized. This evaluation requires us to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that (i) the delivered item has value to the customer on a standalone basis and (ii) if the arrangement includes a general right of return with respect to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in our control. In assessing whether an item has standalone value, we consider factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, we consider whether the collaboration partner can use any other deliverable for its intended purpose without the receipt of the remaining deliverable, whether the value of the deliverable is dependent on the undelivered item, and whether there are other vendors that can provide the undelivered items.

The consideration received under an arrangement that is fixed or determinable is then allocated among the separate units of accounting based on the relative selling prices of the separate units of accounting. We determine the selling price of a unit of accounting within each arrangement using vendor-specific objective evidence of selling price, if available; third-party evidence of selling price if vendor-specific objective evidence is not available; or best estimate of selling price, if neither vendor-specific objective evidence nor third-party evidence is available. Determining the best estimate of selling price for a unit of accounting requires significant judgment. In developing the best estimate of selling price for a unit of accounting, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. We validate the best estimate of selling price for units of accounting by evaluating whether changes in the key assumptions used to determine the best estimate of selling price will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

We recognize arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria are satisfied for that particular unit of accounting. In the event that a deliverable does not represent a separate unit of accounting, we recognize revenue from the combined unit of accounting over the contractual or estimated performance period for the undelivered items, which is typically the term of our research and development obligations. If there is no discernible pattern of performance or objectively measurable performance measures do not exist, then we recognize revenue under the arrangement on a straight-line basis over the period we are expected to satisfy our performance obligations. Conversely, if the pattern of performance over which the service is provided to the customer can be determined and objectively measurable performance measures exist, then we recognize revenue under the arrangement using the proportional performance method. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method or proportional performance method, as applicable, as of the period ending date.

Significant management judgment is required in determining the level of effort required under an arrangement and the period over which we are expected to complete our performance obligations under an arrangement. Steering committee services that are not inconsequential or perfunctory and that are determined to be performance obligations are combined with other research services or performance obligations required under an arrangement, if any, in determining the level of effort required in an arrangement and the period over which we expect to complete our aggregate performance obligations.

Milestone Revenue

Our collaboration and license agreements include contingent milestone payments related to specific development, regulatory and sales-based milestones. Development and regulatory milestones are typically payable when a product candidate initiates or advances in clinical trial phases, upon submission for marketing approval with regulatory authorities, and upon receipt of actual marketing approvals for a therapeutic or for additional indications. Sales-based milestones are typically payable when annual sales reach specified levels.

We evaluate whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (i) the consideration is commensurate with either our performance to achieve the milestone or the enhancement of the value of the delivered item as a result of a specific outcome resulting from our performance to achieve the milestone, (ii) the consideration relates solely to past performance, and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone and the level of effort and investment required to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. We will recognize revenue in its entirety upon successful accomplishment of any substantive milestones, assuming all other revenue recognition criteria are met. Milestones that are not considered substantive are recognized as earned if there are no remaining performance obligations or over the remaining period of performance, with a cumulative catch-up being recognized for the elapsed portion of the period of performance, assuming all other revenue recognition criteria are met.

Non-refundable research, development and regulatory milestones that are expected to be achieved as a result of our efforts during the period of our performance obligations under the collaboration and license agreements are generally considered to be substantive and are recognized as revenue upon the achievement of the milestone, assuming all other revenue recognition criteria are met. If not considered to be substantive, revenue from achievement of milestones is initially deferred and recognized over the remaining term of our performance obligations. Milestones that are not considered substantive because we do not contribute effort to their achievement are recognized as revenue upon achievement, assuming all other revenue recognition criteria are met, as there are no undelivered elements remaining and no continuing performance obligations on our part.

Amounts received prior to satisfying the revenue recognition criteria listed above are recorded as deferred revenue in the accompanying balance sheets. Although we follow detailed guidelines in measuring revenue, certain judgments affect the application of our revenue policy. For example, in connection with our existing collaboration agreements, we have recorded on the balance sheet short-term and long-term deferred revenue based on our best estimate of when such revenue will be recognized. However, this estimate is based on our current research plan and,

if our research plan should change in the future, we may recognize a different amount of deferred revenue over the following 12-month period.

The estimate of deferred revenue also reflects management's estimate of the periods of our involvement in the collaborations. Our primary performance obligations under these collaborations consist of research and development services. In certain instances, the timing of satisfying these obligations can be difficult to estimate. Accordingly, our estimates may change in the future. Such changes to estimates would result in a change in prospective revenue recognition amounts. If these estimates and judgments change over the course of our collaborative agreement, it may affect the timing and amount of revenue that we will recognize and record in future periods.

Equity-Based Compensation

We measure employee equity-based compensation based on the grant date fair value of the equity awards using the Black-Scholes option pricing model. Equity-based compensation expense is recognized on a straight-line basis over the requisite service period of the awards and is adjusted for pre-vesting forfeitures in the period in which the forfeitures occur. For equity awards that have a performance condition, we recognize compensation expense based on our assessment of the probability that the performance condition will be achieved.

We measure equity awards granted to consultants and non-employees based on the fair value of the award on the date of vesting, which is generally the date on which goods or services are received. Compensation expense is recognized over the period during which services are rendered by such consultants and non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of our common stock.

We classify equity-based compensation expense in our consolidated statement of operations in the same manner in which the award recipient's salary and related costs are classified or in which the award recipient's service payments are classified.

Recent Accounting Pronouncements

Please read Note 2 to our consolidated financial statements included in Part IV, Item 15, "Notes to Consolidated Financial Statements," of this annual report on Form 10-K for a description of recent accounting pronouncements applicable to our business.

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 7A. 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 December 31, 2017, we had cash equivalents of $330.9 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. Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our results of operations during the year ended December 31, 2017.

Item 8. Financial Statements and Supplementary Data

The information required by this item is presented at the end of this report beginning on page F-1.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Disclosure Controls and Procedures

The Company has established disclosure controls and procedures designed to ensure that information required to be disclosed in the reports that the Company files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and is accumulated and communicated to management, including the principal executive officer (our Chief Executive Officer) and principal financial officer (our Chief Financial Officer), to allow timely decisions regarding required disclosure.

Our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. 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 December 31, 2017.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2017. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control—Integrated Framework* (2013 framework) (COSO). Based on its

assessment, management believes that, as of December 31, 2017, our internal control over financial reporting is effective based on those criteria.

Changes in Internal Controls 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 December 31, 2017 that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K and is incorporated by reference from our definitive proxy statement relating to our 2018 annual meeting of stockholders, pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended, also referred to in this Annual Report on Form 10-K as our 2018 Proxy Statement, which we expect to file with the SEC no later than May 1, 2018.

Item 10. Directors, Executive Officers and Corporate Governance

Information regarding our directors, including the audit committee and audit committee financial experts, and executive officers and compliance with Section 16(a) of the Exchange Act will be included in our 2018 Proxy Statement and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics for all of our directors, officers and employees as required by Nasdaq governance rules and as defined by applicable SEC rules. Stockholders may locate a copy of our Code of Business Conduct and Ethics on our website at www.intelliatx.com or request a copy without charge from:

Intellia Therapeutics, Inc.
Attention: Investor Relations
40 Erie Street, Suite 130
Cambridge, MA 02139

We will post to our website any amendments to the Code of Business Conduct and Ethics, and any waivers that are required to be disclosed by the rules of either the SEC or Nasdaq.

Item 11. Executive Compensation

The information required by this item regarding executive compensation will be included in our 2018 Proxy Statement and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item regarding security ownership of certain beneficial owners and management and securities authorized for issuance under equity compensation plans will be included in our 2018 Proxy Statement and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item regarding certain relationships and related transactions and director independence will be included in our 2018 Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

The information required by this item regarding principal accounting fees and services will be included in our 2018 Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) The following documents are included in this Annual Report on Form 10-K:

1. The following Report and Consolidated Financial Statements of the Company are included in this Annual Report:

   Report of Independent Registered Public Accounting Firm

   Consolidated Balance Sheets

   Consolidated Statements of Operations

   Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

   Consolidated Statements of Cash Flows

   Notes to Consolidated Financial Statements

2. All financial schedules have been omitted because the required information is either presented in the consolidated financial statements or the notes thereto or is not applicable or required.

3. The exhibits required by Item 601 of Regulation S-K and Item 15(b) of this Annual Report on Form 10-K are listed in the Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K. The exhibits listed in the Exhibit Index are incorporated by reference herein.

Item 16. Form 10-K Summary

The Company has elected not to include summary information.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Intellia Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Intellia Therapeutics, Inc. and subsidiary (the "Company") as of December 31, 2017 and 2016, the related consolidated statements of operations, convertible preferred stock and stockholders' equity (deficit), and cash flows, for each of the three years in the period ended December 31, 2017, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 14, 2018

We have served as the Company's auditor since 2015

INTELLIA THERAPEUTICS, INC.
CONSOLIDATED BALANCE SHEETS
(Amounts in thousands except share and per share data)

	December 31, 2017	December 31, 2016
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 340,678	$ 273,064
Accounts receivable	10,471	6,454
Prepaid expenses and other current assets	3,681	1,788
Total current assets	354,830	281,306
Property and equipment, net	15,272	10,628
Other assets	6,133	7,035
Total Assets	$ 376,235	$ 298,969
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$ 2,172	$ 4,652
Accrued expenses	7,999	5,900
Current portion of deferred revenue	21,188	20,178
Total current liabilities	31,359	30,730
Deferred revenue, net of current portion	44,111	58,109
Other long-term liabilities	168	293
Commitments and contingencies (Note 6)		
Stockholders' Equity:		
Common stock, $0.0001 par value; 120,000,000 shares authorized; 42,384,623 shares issued and outstanding and 36,018,540 shares issued and outstanding, respectively	4	4
Additional paid-in capital	421,706	263,403
Accumulated deficit	(121,113)	(53,570)
Total stockholders' equity	300,597	209,837
Total Liabilities and Stockholders' Equity	$ 376,235	$ 298,969

See notes to consolidated financial statements.

INTELLIA THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(Amounts in thousands except per share data)

	Year Ended December 31,		
	2017	2016	2015
Collaboration revenue	$ 26,117	$ 16,479	$ 6,044
Operating expenses:			
Research and development	67,647	31,840	11,170
General and administrative	28,025	16,798	8,283
Total operating expenses	95,672	48,638	19,453
Operating loss	(69,555)	(32,159)	(13,409)
Interest income	2,012	525	-
Loss before income taxes	(67,543)	(31,634)	(13,409)
Income tax benefit	-	-	1,012
Net loss	$ (67,543)	$ (31,634)	$ (12,397)
Net loss per share, basic and diluted	$ (1.88)	$ (1.42)	$ (51.02)
Weighted average shares outstanding, basic and diluted	36,006	22,222	243

See notes to consolidated financial statements.

INTELLIA THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(Amounts in thousands, except unit and share data)

	Series A-1, Series A-2 and Junior Preferred		Common		Common		Incentive		Additional Paid-In	Accumulated	Total Stockholders' Equity (Deficit	Convertible Preferred Stock	
	Units	Amount	Units	Amount	Shares	Amount	Units	Amount	Capital	Deficit	)	Shares	Amount
Balance at December 31, 2014	19,348,694	16,448	2,298,000	607	-	-	1,558,498	50	-	(9,539)	7,566	-	-
Issuance of Class A-2 Preferred Units net of issuance costs of $16	1,333,333	1,984	-	-	-	-	-	-	-	-	1,984	-	-
Allocation from Novartis collaboration to carrying value of Preferred Shares	-	2,644	-	-	-	-	-	-	-	-	2,644	-	-
Tax provision associated with intraperiod tax allocation	-	(1,012)	-	-	-	-	-	-	-	-	(1,012)	-	-
Effect of Reorganization	(20,682,027)	(20,064)	(2,298,000)	(607)	1,713,104	-	(1,558,498)	(50)	50	-	(20,671)	22,980,027	20,671
Issuance of Series B Preferred Shares, net of issuance costs of $2,754	-	-	-	-	-	-	-	-	-	-	-	13,336,601	67,263
Equity-based compensation	-	-	-	-	845,651	-	-	-	685	-	685	-	623
Net loss	-	-	-	-	-	-	-	-	-	(12,397)	(12,397)	-	-
Balance at December 31, 2015	-	-	-	-	2,558,755	-	-	-	735	(21,936)	(21,201)	36,316,628	88,557
Conversion of convertible preferred stock	-	-	-	-	23,481,956	3	-	-	88,554	-	88,557	(36,316,628)	(88,557)
Issuance of common stock net of issuance costs of $3,367	-	-	-	-	9,955,554	1	-	-	167,138	-	167,139	-	-
Exercise of stock options	-	-	-	-	257	-	-	-	2	-	2	-	-
Issuance of shares under employee stock purchase plan	-	-	-	-	23,209	-	-	-	259	-	259	-	-
Equity-based compensation	-	-	-	-	(1,191)	-	-	-	6,715	-	6,715	-	-
Net loss	-	-	-	-	-	-	-	-	-	(31,634)	(31,634)	-	-
Balance at December 31, 2016	-	-	-	-	36,018,540	4	-	-	263,403	(53,570)	209,837	-	-
Issuance of common stock	-	-	-	-	6,250,000	-	-	-	141,000	-	141,000	-	-
Exercise of stock options	-	-	-	-	141,759	-	-	-	1,156	-	1,156	-	-
Issuance of shares under employee stock purchase plan	-	-	-	-	64,786	-	-	-	825	-	825	-	-
Equity-based compensation	-	-	-	-	(90,462)	-	-	-	15,322	-	15,322	-	-
Net loss	-	-	-	-	-	-	-	-	-	(67,543)	(67,543)	-	-
Balance at December 31, 2017	-	$ -	-	$ -	42,384,623	$ 4	-	$ -	$ 421,706	$ (121,113)	$ 300,597	-	$ -

INTELLIA THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(Amounts in thousands)

	Year Ended December 31,		
	2017	**2016**	**2015**
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (67,543)	$ (31,634)	$ (12,397)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:			
Depreciation and amortization	2,994	1,104	328
Loss on disposal of property and equipment	166	13	9
Equity-based compensation	15,322	6,715	1,308
Changes in operating assets and liabilities:			
Accounts receivable	(4,017)	(5,454)	(1,012)
Prepaid expenses and other current assets	(1,893)	(979)	(525)
Accounts payable	(488)	1,784	335
Accrued expenses	2,394	3,050	805
Deferred revenue	(12,988)	67,975	9,312
Other assets	902	(6,435)	(76)
Other long-term liabilities	(125)	(30)	150
Net cash (used in) provided by operating activities	(65,276)	36,109	(1,763)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchases of property and equipment	(10,091)	(6,165)	(2,554)
Net cash used in investing activities	(10,091)	(6,165)	(2,554)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from sale of Class A-1 and A-2 preferred units and Series B preferred stock	-	-	74,661
Payments to acquire in-process research and development	-	(600)	(1,100)
Payment of preferred unit and preferred stock issuance costs	-	(100)	(2,671)
Proceeds from common stock offering	141,000	170,507	-
Proceeds from options exercised	1,156	2	-
Issuance of shares through employee stock purchase plan	825	259	-
Payment of common stock offering costs	-	(2,764)	(602)
Net cash provided by financing activities	142,981	167,304	70,288
Net increase in cash and cash equivalents	67,614	197,248	65,971
Cash and cash equivalents, beginning of period	273,064	75,816	9,845
Cash and cash equivalents, end of period	$ 340,678	$ 273,064	$ 75,816
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:			
Purchases of property and equipment unpaid at period end	$ 805	$ 3,090	$ 219
Acquisition of in-process research and development unpaid at period end	-	-	600
Financing costs incurred but unpaid at period end	-	-	970
Conversion of convertible preferred stock to common stock	-	88,557	-

See notes to consolidated financial statements.

1. The Company

Intellia Therapeutics, Inc. ("Intellia" or the "Company") is a genome editing company focused on developing curative therapeutics utilizing a biological tool known as CRISPR/Cas9.

The Company commenced active operations in mid-2014. Since its inception, the Company has generated an accumulated deficit of $121.1 million through December 31, 2017 and will require substantial additional capital to fund its research and development. The Company is subject to risks and uncertainties common to early stage companies in the biotechnology industry, including, but not limited to, development by competitors of more advanced or effective therapies, dependence on key executives, protection of and dependence on proprietary technology, compliance with government regulations and ability to secure additional capital to fund operations. Programs currently under development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

2. Summary of Significant Accounting Policies

Basis of Presentation

The 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.

Use of Estimates

The preparation of the Company's consolidated financial statements in accordance with accounting principles generally accepted in the United States of America ("U.S.") requires management to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities as of the date of the consolidated financial statements and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, revenue recognition and the valuation of common and incentive units for the periods prior to the Company's stock becoming publicly traded. Estimates are periodically reviewed in light of changes in circumstances, facts and experiences. Actual results may differ materially from management's estimates, judgments and assumptions.

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 December 31, 2017 and 2016 consisted primarily of cash and cash equivalents, accounts receivable and accounts payable. As of December 31, 2017 and 2016, the Company's financial assets recognized at fair value consisted of the following:

	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	$ -	$ -

	Fair Value as of December 31, 2016			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	$ 270,448	$ 270,448	$ -	$ -
Total	$ 270,448	$ 270,448	$ -	$ -

The Company values its cash equivalents at 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.

Cash Equivalents

The Company considers all highly liquid investments with maturities of three months or less when purchased to be cash equivalents. As of December 31, 2017 and 2016, cash equivalents consisted of interest-bearing money market accounts, commercial paper and U.S. treasury securities.

Concentrations of Credit Risk

The Company's cash and cash equivalents may potentially be subject to concentrations of credit risk. The Company generally maintains balances in various accounts in excess of federally insured limits with financial institutions that management believes to be of high credit quality.

Accounts receivable represent amounts due from collaboration partners. The Company monitors economic conditions to identify facts or circumstances that may indicate that any of its accounts receivable are at risk of collection. As of December 31, 2017 and 2016, the Company's two collaboration partners, Regeneron Pharmaceuticals, Inc. ("Regeneron") and Novartis Institutes for BioMedical Research, Inc. ("Novartis"), accounted for all of the Company's accounts receivable.

Property and Equipment

The Company records property and equipment at cost and recognizes depreciation and amortization using the straight-line method over the following estimated useful lives of the respective assets:

Asset Category	Useful Life
Laboratory equipment	5 years
Office furniture and equipment	5 years
Computer software	3 years
Computer equipment	3 years
Leasehold improvements	5 years or term of respective lease, if shorter

Expenditures for repairs and maintenance of assets are expensed as incurred. Upon retirement or sale, the cost of assets disposed and the corresponding accumulated depreciation are removed from the related accounts and any resulting gain or loss is reflected in the results of operations.

Impairment of Long-Lived Assets

The Company tests long-lived assets to be held and used, including property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying amount of assets or asset groups may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets.

Evaluation of recoverability of the asset or asset group is based on an estimate of undiscounted future cash flows resulting from the use of the asset or asset group and its eventual disposition. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the asset or asset group, the assets are written down to their estimated fair values. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. To date, the Company has not recorded any material impairment losses on long-lived assets.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences attributable to differences between carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax reporting purposes and for operating loss and tax credit carryforwards. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes.

The Company's deferred tax assets and liabilities are measured using enacted tax rates expected to apply in the years in which these temporary differences are expected to be recovered or settled. A valuation allowance is recorded to reduce deferred tax assets if it is determined that it is more likely than not that all or a portion of the deferred tax asset will not be realized. The Company considers many factors when assessing the likelihood of future realization of deferred tax assets, including recent earnings results, expectations of future taxable income, carryforward periods available and other relevant factors. The Company records changes in the required valuation allowance in the period that the determination is made.

The Company assesses its income tax positions and records tax benefits for all years subject to examination based upon management's evaluation of the facts, circumstances and information available as of the reporting date. For those tax positions where it is more likely than not that a tax benefit will be sustained, the Company records the largest amount of tax benefit with a greater than 50.0% likelihood of being realized upon ultimate settlement with a taxing authority having full knowledge of all relevant information. For those income tax positions where it is not more likely than not that a tax benefit will be sustained, the Company does not recognize a tax benefit in the financial statements. The Company records interest and penalties related to uncertain tax positions, if applicable, as a component of income tax expense.

Revenue Recognition

The Company recognizes revenue for each identified unit of accounting when all of the following criteria are met: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the seller's price to the buyer is fixed or determinable; and collectability is reasonably assured.

The terms of the Company's collaboration and license agreements contain multiple deliverables, which include licenses to CRISPR/Cas9-based therapeutic products directed to specific targets, referred to as exclusive licenses, as well as research and development activities to be performed by the Company on behalf of the collaboration partner related to the licensed targets. Payments that the Company may receive under these types of agreements include non-refundable technology access fees, payments for research activities, payments based upon the achievement of specified milestones and royalties on any resulting net product sales.

Multiple-Element Arrangements

The Company's collaboration and license agreements represent multiple-element arrangements. The Company evaluates its collaborative agreements for proper classification in its statements of operations based on the nature of

the underlying activity. The Company generally reflects as revenue amounts due under its collaborative agreements related to reimbursement of development activities as the Company is generally the principal under the arrangement.

The Company evaluates multiple-element arrangements to determine (i) the deliverables included in the arrangement and (ii) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. When deliverables are separable, consideration received is allocated to the separate units of accounting based on the relative selling price method and the appropriate revenue recognition principles are applied to each unit. When the Company determines that an arrangement should be accounted for as a single unit of accounting, the Company must determine the period over which the various elements will be delivered and revenue will be recognized. This evaluation requires the Company to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that (i) the delivered item has value to the customer on a standalone basis and (ii) if the arrangement includes a general right of return with respect to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the Company's control. In assessing whether an item has standalone value, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can use any other deliverable for its intended purpose without the receipt of the remaining deliverable, whether the value of the deliverable is dependent on the undelivered item, and whether there are other vendors that can provide the undelivered items.

The consideration received under an arrangement that is fixed or determinable is then allocated among the separate units of accounting based on the relative selling prices. The Company determines the selling price of a unit of accounting within each arrangement using vendor-specific objective evidence of selling price, if available; third-party evidence of selling price if vendor-specific objective evidence is not available; or best estimate of selling price, if neither vendor-specific objective evidence nor third-party evidence is available. Determining the best estimate of selling price for a unit of accounting requires significant judgment. In developing the best estimate of selling price for a unit of accounting, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company validates the best estimate of selling price for units of accounting by evaluating whether changes in the key assumptions used to determine the best estimate of selling price will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

The Company recognizes arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria are satisfied for that particular unit of accounting. In the event that a deliverable does not represent a separate unit of accounting, the Company recognizes revenue from the combined unit of accounting over the contractual or estimated performance period for the undelivered items, which is typically the term of the Company's research and development obligations. If there is no discernible pattern of performance or objectively measurable performance measures do not exist, then the Company recognizes revenue under the arrangement on a straight-line basis over the period the Company is expected to satisfy its performance obligations. Conversely, if the pattern of performance over which the service is provided to the customer can be determined and objectively measurable performance measures exist, then the Company recognizes revenue under the arrangement using the proportional performance method. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method or proportional performance method, as applicable, as of the period ending date.

Significant management judgment is required in determining the level of effort required under an arrangement and the period over which the Company is expected to complete its performance obligations under an arrangement. Steering committee services that are not inconsequential or perfunctory and that are determined to be performance obligations are combined with other research services or performance obligations required under an arrangement, if any, in determining the level of effort required in an arrangement and the period over which the Company expects to complete its aggregate performance obligations.

Milestone Revenue

The Company's collaboration and license agreements include contingent milestone payments related to specific development, regulatory and sales-based milestones. Development and regulatory milestones are typically payable when a product candidate initiates or advances in clinical trial phases, upon submission for marketing approval with

regulatory authorities, and upon receipt of actual marketing approvals for a therapeutic or for additional indications. Sales-based milestones are typically payable when annual sales reach specified levels.

The Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (i) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item as a result of a specific outcome resulting from the Company's performance to achieve the milestone, (ii) the consideration relates solely to past performance, and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone and the level of effort and investment required to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. The Company will recognize revenue in its entirety upon successful accomplishment of any substantive milestones, assuming all other revenue recognition criteria are met. Milestones that are not considered substantive are recognized as earned if there are no remaining performance obligations or over the remaining period of performance, with a cumulative catch-up being recognized for the elapsed portion of the period of performance, assuming all other revenue recognition criteria are met.

Non-refundable research, development and regulatory milestones that are expected to be achieved as a result of the Company's efforts during the period of its performance obligations under the collaboration and license agreements may be considered to be substantive and are recognized as revenue upon the achievement of the milestone, assuming all other revenue recognition criteria are met. If not considered to be substantive, revenue from achievement of milestones is initially deferred and recognized over the remaining term of its performance obligations. Milestones that are not considered substantive because the Company does not contribute effort to their achievement are recognized as revenue upon achievement, assuming all other revenue recognition criteria are met, as there are no undelivered elements remaining and no continuing performance obligations on the Company's part.

Amounts received prior to satisfying the revenue recognition criteria listed above are recorded as deferred revenue in the accompanying balance sheets. Although the Company follows detailed guidelines in measuring revenue, certain judgments affect the application of the Company's revenue policy. For example, in connection with its existing collaboration agreements, the Company has recorded on its balance sheet short-term and long-term deferred revenue based on its best estimate of when such revenue will be recognized. However, this estimate is based on the Company's current research plan and, if its research plan should change in the future, the Company may recognize a different amount of deferred revenue over the following 12-month period.

The estimate of deferred revenue also reflects management's estimate of the periods of the Company's involvement in its collaborations. The Company's primary performance obligations under these collaborations consist of research and development services. In certain instances, the timing of satisfying these obligations can be difficult to estimate. Accordingly, the Company's estimates may change in the future. Such changes to estimates would result in a change in prospective revenue recognition amounts. If these estimates and judgments change over the course of any of the Company's collaborative agreements, it may affect the timing and amount of revenue that the Company will recognize and record in future periods.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development expenses consist of salaries, equity-based compensation and benefits of employees, lab supplies and materials, facilities expenses, overhead expenses, fees paid to subcontractors and contract research organizations and other external expenses.

The Company records payments made for research and development services prior to the services being rendered as prepaid expense on the consolidated balance sheet and expenses them as the services are provided. Contracts for multi-year research and development services are recorded on a straight-line basis over each annual contractual period based on the total contractual fee when the services rendered are expected to be substantially equivalent over the term of the arrangement. The cost of obtaining licenses for certain technology or intellectual property is recorded to research and development expense when incurred if the licensed technology or intellectual property has not yet reached technological feasibility and has no alternative future use.

Equity-Based Compensation

The Company measures employee equity-based compensation based on the grant date fair value of the equity awards using the Black-Scholes option pricing model. Equity-based compensation expense is recognized on a straight-line basis over the requisite service period of the awards and is adjusted for pre-vesting forfeitures in the period in which the forfeitures occur. For equity awards that have a performance condition, the Company recognizes compensation expense based on its assessment of the probability that the performance condition will be achieved.

The Company measures equity awards granted to consultants and non-employees based on the fair value of the award on the date each portion of the award vests, which represents when the Company receives the related goods or services. Compensation expense is recognized over the period during which services are rendered by such consultants and non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of that equity award.

The Company classifies equity-based compensation expense in its consolidated statement of operations in the same manner in which the award recipient's salary and related costs are classified or in which the award recipient's service payments are classified.

(Loss) Earnings per Share

The Company calculates basic (loss) earnings per share by dividing (loss) income allocable to common stockholders by the weighted average number of common shares outstanding. During periods of income, the Company allocates to participating securities a proportional share of income determined by dividing total weighted average participating securities by the sum of the total weighted average common shares and participating securities (the "two-class method"). The Company's preferred stock and restricted common stock have rights to earnings and to participate in distributions of the Company and are therefore considered to be participating securities. Participating securities have the effect of diluting both basic and diluted earnings per share during periods of income. During periods of loss, the Company allocates no loss to preferred units or preferred stock because they have no contractual obligation to share in the losses of the Company. The Company computes diluted (loss) earnings per share after giving consideration to the dilutive effect of stock options that are outstanding during the period, except where such non-participating securities would be anti-dilutive.

Segment Information

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company's one business segment is the development of gene editing-based therapies. All of the Company's assets are held in the U.S. and all of the Company's revenue has been generated in the U.S.

Recent Accounting Pronouncements

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 supersedes existing revenue recognition guidance. The standard's core principle is that a company will recognize revenue when it transfers promised goods or services to future, potential customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. The standard defines a five-step process to achieve this principle and will require companies to use more judgment and make more estimates than under the current guidance. These judgments and estimates will include identifying performance obligations in the customer contract, estimating the amount of variable consideration to include in the transaction price, and allocating the transaction price to each separate performance obligation. ASU 2014-09 also requires additional disclosure about the nature, amount, timing, and uncertainty of revenue and cash flows arising from customer contracts. The Company's collaboration agreements with Novartis and Regeneron, which are discussed further in Note 7, are its sole sources of revenue and the only arrangements affected by the adoption of the new standard.

The Company will adopt the new standard effective January 1, 2018 under the modified retrospective method. During the fourth quarter of 2017, the Company substantially completed its assessment of the impact that the new standard will have on its consolidated financial statements. The Company preliminarily expects that the most significant impact of adopting the new standard relates to the treatment of quarterly research payments due to the

Company under the collaboration with Novartis, as discussed further in Note 7. Under current generally accepted accounting principles, or GAAP, the Company does not account for these payments until the period they are received as they are not considered determinable. Under the new standard, the Company will include an estimate of variable consideration related to the quarterly research payments in the transaction price at the inception of the arrangement. The Company preliminarily expects that this change would have resulted in the recognition of additional revenue of approximately $5.4 million through December 31, 2017, which will be reflected as a credit to accumulated deficit on January 1, 2018. The Company preliminarily expects that revenue recognition related to the collaboration with Regeneron, as discussed further in Note 7, will remain substantially unchanged.

In February 2016, the FASB issued ASU No. 2016-02, *Leases*. ASU 2016-02 amends ASC 840, *Leases*, by introducing a lessee model that requires balance sheet recognition of most leases. 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 is evaluating the impact that the adoption of ASU 2016-02 will have on its consolidated financial statements but expects that the Company will recognize a significant lease obligation upon adoption. See Note 6 for additional information related to the Company's lease obligations.

3. Property and Equipment, Net

Property and equipment, net consisted of the following:

	December 31,	
	2017	2016
	(in thousands)	
Laboratory equipment	$ 16,704	$ 9,901
Office furniture and equipment	960	690
Computer equipment	845	703
Leasehold improvements	656	616
Computer software	436	148
Property and equipment	19,601	12,058
Less: accumulated depreciation and amortization	(4,329)	(1,430)
Property and equipment, net	$ 15,272	$ 10,628

Depreciation and amortization expense was $3.0 million, $1.1 million and $0.3 million for the years ended December 31, 2017, 2016 and 2015, respectively.

4. Accrued Expenses

Accrued expenses consisted of the following:

	December 31, 2017	December 31, 2016
	(In thousands)	
Employee compensation and benefits	$ 4,773	$ 2,703
Research and development and professional expenses	3,226	3,197
Accrued expenses	$ 7,999	$ 5,900

5. Income Taxes

The Company did not record net income tax benefits for the operating losses incurred during the periods presented due to the uncertainty of realizing a tax benefit from those losses. Accordingly, any benefit recorded related to these deferred tax assets was offset by a valuation allowance reflecting management's conclusion that realization of those assets was not more likely than not.

Intraperiod tax allocation rules require the allocation of the provision for income taxes between continuing operations and other categories of earnings, such as items credited directly to members' equity. In periods in which the Company has a year-to-date pre-tax loss from continuing operations and has pre-tax income in other categories of earnings, the Company must allocate the income tax provision to the other categories of earnings. The Company then records a related income tax benefit in continuing operations.

During the year ended December 31, 2015, the Company allocated $2.6 million from the $30.0 million total fixed amount of consideration under the collaboration agreement with Novartis to the carrying value of the Class A-1 and A-2 Preferred Units to record those units based on their fair value at date of issuance. As a result of this allocation, during the year ended December 31, 2015, the Company recorded an income tax provision of $1.0 million within members' equity as well as a corresponding income tax benefit of $1.0 million within continuing operations. Refer to Note 7, *Collaborations*, for additional information regarding this difference in value.

A reconciliation of the federal statutory income tax rate and the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2017	2016	2015
Federal statutory income tax rate	(34.0)%	(34.0)%	(34.0)%
State income taxes	(6.9)	(6.7)	(4.4)
Intraperiod tax allocation	-	-	(6.7)
Permanent items	-	-	2.2
Research and development tax credits	(3.4)	(2.8)	(1.8)
Stock-based compensation	3.6	1.9	1.1
Change in U.S. tax rate	18.7	-	-
Change in valuation allowance	22.0	41.6	36.0
Effective income tax rate	-%	-%	(7.6)%

The Company's net deferred tax assets (liabilities) consisted of the following:

	December 31,	
	2017	2016
	(in thousands)	
Deferred tax assets:		
Intangibles, including acquired in-process research and development	$ 1,303	$ 2,035
Capitalized start-up costs	502	785
Net operating loss carryforwards	9,406	13,751
Research and development credit carryforwards	5,817	1,873
Deferred revenue	15,913	1,193
Equity-based compensation	3,248	1,940
Accruals and allowances	1,112	1,139
Gross deferred tax assets	37,301	22,716
Deferred tax asset valuation allowance	(35,372)	(20,549)
Total deferred tax assets	1,929	2,167
Deferred tax liabilities:		
Fixed assets	(1,929)	(2,167)
Total deferred tax liabilities	(1,929)	(2,167)
Net deferred tax asset (liability)	$ -	$ -

As of December 31, 2017, the Company had federal and state net operating loss carryforwards of $36.7 million and $27.8 million, respectively, which begin to expire in 2034. As of December 31, 2017, the Company had federal and state research and development tax credit carryforwards of approximately $3.4 million and $2.5 million, which begin to expire in 2034 and 2030, respectively.

The Company evaluated the expected realizability of its net deferred tax assets as of December 31, 2017 and 2016 and determined that there was significant negative evidence due to its net operating loss position and insufficient positive evidence to support the realizability of these net deferred tax assets. The Company concluded it is more likely than not that its net deferred tax assets would not be realized in the future; therefore, the Company has provided a full valuation allowance against its net deferred tax asset balance as of December 31, 2017 and 2016. The valuation allowance increased by $14.8 million in 2017, $13.1 million in 2016 and $3.8 million in 2015.

Utilization of the net operating loss and research and development credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of net operating loss and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax expense, respectively. The Company has not yet conducted a study to assess whether a change of control, as defined in Section 382, has occurred or whether there have been multiple changes in control since inception.

As of December 31, 2017, the Company had not identified any unrecognized tax benefits. The Company files income tax returns in the U.S. federal tax jurisdiction and Massachusetts and various other state tax jurisdictions. The Company is subject to examination by the Internal Revenue Service and Massachusetts taxing authorities. The returns in these jurisdictions since inception remain open for examination; however, there are currently no pending tax examinations.

On December 22, 2017, the Tax Cuts and Jobs Act ("TCJA") was enacted. This law substantially amended the Internal Revenue Code and among other things, permanently reduced the U.S. corporate income tax rate from 35% to 21%. On December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act ("SAB 118"), which allows the recording of provisional amounts during a measurement period not to extend beyond one year of the enactment date. As a result of remeasuring the deferred tax assets and liabilities to the lower tax rate, the net deferred tax assets decreased by $12.6 million, which was offset by a decrease in the valuation allowance. In accordance with SAB 118, the amount the Company recorded is a provisional amount and a reasonable estimate at December 31, 2017. The final impact may differ from this provisional amount due to, among other things, changes in interpretations and assumptions the Company has made thus far and the issuance of additional regulatory or other guidance. The Company expects to complete the measurement of the final impact within the one year measurement period.

6. Commitments and Contingencies

Commitments

Property Leases

In October 2014, the Company entered into an agreement to lease office and laboratory space in Cambridge, Massachusetts under an operating lease agreement with a term through January 2020, with an option to extend the term of the lease for an additional five-year period. Upon the execution of this lease, the Company provided a $0.3 million security deposit. The Company has recorded this security deposit in other assets on the consolidated balance sheets. In January 2016, the Company entered into a ten-year agreement to lease office and laboratory space in Cambridge, Massachusetts under an operating lease agreement, with an option to terminate the lease at the end of the sixth year and an option to extend the term of the lease for an additional three years. Upon the execution of this lease, the Company provided a $2.2 million security deposit, which has been recorded in other assets on the consolidated balance sheets. In addition, the Company had prepaid $3.3 million in lease payments as of December 31, 2017 under the terms of this lease.

The Company recognizes rent expense, inclusive of escalation charges, on a straight-line basis over the initial term of the lease agreements. The Company recorded rent expense of $6.0 million, $2.7 million and $0.6 million during the years ended December 31, 2017, 2016 and 2015, respectively.

Future minimum lease payments under the Company's property leases as of December 31, 2017 are as follows:

Year Ending December 31,	(In thousands)
2018	$ 5,453
2019	5,616
2020	4,963
2021	5,507
2022	3,861
Thereafter	-
	$ 25,400

Contingencies

In connection with a July 2014 intellectual property license with Caribou Biosciences, Inc. ("Caribou"), a stockholder who held 10.7% of the Company's common stock at December 31, 2017, the Company gained access to sublicensed intellectual property from various academic and professional institutions. Under these sublicenses, the Company may be obligated to pay development and regulatory milestones of up to $6.4 million, sales-based milestones of up to $20.0 million and up to mid-single-digit royalties on net sales of any products covered by issued patents to these entities in certain circumstances.

Under the Caribou license agreement, the Company sublicenses a patent family that has been subject to interference proceedings declared by the Patent Trial and Appeal Board of the U.S. Patent and Trademark Office ("PTAB"). These interference proceedings were dismissed by the PTAB on February 15, 2017, and, as a result, potential claims may be asserted against the Company during the development or commercialization of a product that relies on the technology underlying this patent family. Defense of any such claims would involve substantial litigation expense, and any successful claim of infringement against the Company could require it to pay substantial damages.

7. Collaborations

Novartis Institutes for BioMedical Research

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

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 collaboration 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 at least one 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 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 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. 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 December 31, 2017, 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 $34.4 million in cash and accounts receivable under the Novartis agreement. Through December 31, 2017, the Company has recognized $23.1 million of collaboration revenue, including $9.3 million in the year ended December 31, 2017, $7.8 million in the year ended December 31, 2016, and $6.0 million in year ended December 31, 2015, in the consolidated statements of operations related to this agreement. As of December 31, 2017 and 2016, the Company had accounts receivable of $6.0 million and $6.0 million, respectively, related to this agreement. As of December 31, 2017 and 2016, the Company had deferred revenue of $11.2 million and $11.6 million, respectively, related to this agreement.

Regeneron Pharmaceuticals, Inc.

In April 2016, the Company entered into a license and collaboration 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 gene 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 gene 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 will be 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 may be 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 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 initial investigational new drug ("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 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 single-digit royalty obligations under a license agreement with Caribou Biosciences, Inc. ("Caribou"). In addition, Regeneron is obligated to fund 50.0% of the research and development costs for the transthyretin amyloidosis program, the first target selected by Regeneron, which will be subject to a co-development and co-commercialization arrangement between the Company and Regeneron.

The fixed portion of consideration under the collaboration arrangement was determined to be the $75.0 million nonrefundable upfront payment, for which there are no contingent terms. The significant deliverables of this multiple-element revenue arrangement were determined to be licenses to targets, the associated research activities and evaluation plans for these programs and the technology collaboration. The Company further determined that the licenses and associated research activities and evaluation plans did not have standalone value due to the specialized nature of the services to be provided by the Company; therefore, these deliverables are not separable, and, accordingly, the license and services are treated as a single unit of accounting. The Company additionally concluded that the technology collaboration has standalone value from the product development, as shared rights to technological advancements under the technology collaboration could be separately applied by Regeneron to other programs.

The Company allocated the $75.0 million in fixed consideration to the two units of accounting based on the estimated relative selling price of each deliverable. The Company estimated the selling price of each deliverable 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 licenses to targets and the associated research activities and evaluation plans and $11.2

million to the technology collaboration. The $63.8 million allocated to the licenses to targets and the associated research activities and evaluation plans for these programs is being recognized over the six-year performance period of the arrangement. The $11.2 million allocated to the technology collaboration is being recognized over a period beginning with the inception of the technology collaboration in September 2016, through the end of the arrangement.

Collaboration Revenue

Through December 31, 2017, the Company recorded a $75.0 million upfront payment and $4.6 million for research and development services under the Regeneron agreement. The Company recognized $16.8 million and $8.7 million of collaboration revenue in the years ended December 31, 2017 and 2016, respectively, in the consolidated statements of operations. As of December 31, 2017 and 2016, the Company had deferred revenue of $54.1 million and $66.7 million, respectively, and accounts receivable of $4.5 million and $0.5 million, respectively, related to this agreement.

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.

8. Equity-Based Compensation

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

	Year Ended December 31,		
	2017	2016	2015
	(In thousands)		
Research and development	$ 7,280	$ 4,083	$ 1,061
General and administrative	8,042	2,632	247
Total	$ 15,322	$ 6,715	$ 1,308

Restricted Stock

Restricted stock is measured at the fair value of the underlying security. Prior to the IPO, the Company valued these awards by taking into consideration its most recently available valuation performed by management and the board of directors, considering the most recently available third-party valuations of the Company's securities as well as additional qualitative factors. In the periods subsequent to the IPO, fair value was determined based on the quoted price of the Company's common stock.

The following table summarizes the Company's restricted stock activity, including converted Founder Stock, for the year ended December 31, 2017:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Unvested restricted stock as of December 31, 2016	1,361,855	$ 0.81
Vested	(791,571)	0.69
Forfeited	(90,462)	1.34
Unvested restricted stock as of December 31, 2017	479,822	$ 0.90

As of December 31, 2017, there was $2.5 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 1.0 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 $12.43 per option for options granted during the year ended December 31, 2017, $6.48 per option for options granted during the year ended December 31, 2016 and $4.24 per option for options granted during the year ended December 31, 2015. Key assumptions used to apply this pricing model were as follows:

	Year Ended December 31,		
	2017	2016	2015
Risk-free interest rate	2.0%	1.3%	1.5%
Expected life of options	6.0 years	6.0 years	6.0 years
Expected volatility of underlying stock	93.9%	88.0%	82.6%
Expected dividend yield	0.0%	0.0%	0.0%

The following is a summary of stock option activity for the year ended December 31, 2017:

	Number of Options	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Outstanding at December 31, 2016	3,040,214	$ 8.35		
Granted	2,691,157	16.26		
Exercised	(141,759)	8.16		
Forfeited	(884,164)	12.55		
Outstanding at December 31, 2017	4,705,448	12.09	7.63	35,087
Exercisable at December 31, 2017	1,685,074	9.06	5.26	17,172

As of December 31, 2017, there was $27.2 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 3.1 years.

9. Loss Per Share

Basic and diluted loss per share attributable to common stockholders was calculated as follows:

	Year Ended December 31,		
	2017	2016	2015
	(In thousands)		
Net loss	$ (67,543)	$ (31,634)	$ (12,397)
Weighted average shares outstanding, basic and diluted	36,006	22,222	243
Net loss per share attributable to common stockholders, basic and diluted	$ (1.88)	$ (1.42)	$ (51.02)

In May 2016, the Company issued 6,900,000 shares of common stock in connection with its IPO and 23,481,956 shares of common stock in connection with the automatic conversion of its convertible preferred stock upon the closing of the IPO. In addition, the Company issued a total of 3,055,554 shares of common stock in two separate, concurrent private placements upon the closing of the IPO. The issuance of these shares resulted in a significant increase in the Company's weighted average shares outstanding and has affected the year-over-year comparability of the Company's (loss) earnings per share calculations throughout 2017.

On November 1, 2017, the Company entered into an underwriting agreement related to a public offering of 6,250,000 shares of the Company's common stock, par value $0.0001 per share.

The following common stock equivalents were excluded from the calculation of diluted loss per share in 2017, 2016 and 2015 because their inclusion would have been anti-dilutive:

	Year Ended December 31,		
	2017	2016	2015
	(In thousands)		
Convertible preferred stock	-	-	21,363
Unvested restricted stock	480	1,362	1,945
Stock options	4,705	3,040	456
	5,185	4,402	23,764

10. Stockholders' Equity

On May 11, 2016, the Company completed an initial public offering ("IPO") of its common stock, which resulted in the sale of 6,900,000 shares, including all additional shares available to cover over-allotments, at a price of $18.00 per share. The Company received net proceeds before expenses from the IPO of $115.5 million after deducting underwriting discounts and commissions paid by the Company. In preparation for the IPO, the Company's board of directors and stockholders approved a one-for-1.7 reverse stock split of the Company's common stock effective April 25, 2016. All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted, where necessary, to give effect to this reverse stock split. In connection with the closing of the IPO, all of the Company's outstanding convertible preferred stock automatically converted to common stock at a one-for-0.6465903 ratio as of May 11, 2016, resulting in an additional 23,481,956 shares of common stock of the Company becoming outstanding. In addition, the Company issued a total of 3,055,554 shares of common stock for $55.0 million in two separate, concurrent private placements upon the closing of the IPO.

On November 1, 2017, the Company entered into an underwriting agreement related to a public offering of 6,250,000 shares of the Company's common stock, par value $0.0001 per share. The offering closed on November 6th and the Company received net proceeds of $141.0 million, after deducting underwriting discounts.

Reorganization

In July 2014, Intellia Therapeutics, LLC was formed as the parent company of Intellia Therapeutics, Inc. In August 2015, the Company completed a series of transactions pursuant to which Intellia Therapeutics, LLC merged with and into its C corporation subsidiary, Intellia Therapeutics, Inc., with Intellia Therapeutics, Inc. continuing to exist as the surviving corporation (the "Reorganization"). In connection with the Reorganization, all of the outstanding common and preferred unitholders of Intellia Therapeutics, LLC received shares of preferred stock of Intellia Therapeutics, Inc., and holders of incentive units in Intellia Therapeutics, LLC received shares of restricted common stock in Intellia Therapeutics, Inc. The Company determined that the Reorganization lacked economic substance and should be accounted for in a manner consistent with a common control transaction. Similarly, as there was no change in fair value between stockholders, individually or as a class, the Company determined that the exchange of shares occurring in the Reorganization should be accounted for as a modification of the equity securities and presented as a reclassification of the components of equity.

The Company classifies stock that is redeemable in circumstances outside of the Company's control outside of permanent equity. The Company recorded convertible preferred stock at fair value upon issuance, net of any issuance costs or discounts. No accretion was recognized as the contingent events that could give rise to redemption were not deemed probable. The preferred stock outstanding at December 31, 2015 was automatically converted to common stock in connection with the closing of the IPO.

11. 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 and concurrently licensed certain intellectual property and entered into an arrangement under which Caribou provided research and development services. In addition, under the license agreement the Company agreed to pay 30% of Caribou's patent prosecution, filing and maintenance costs under its intellectual property license agreement with Caribou. As a result of this and subsequent transactions, Caribou owned 10.7% of the Company's voting interests as of December 31, 2017.

During the year ended December 31, 2015, the Company recognized $1.5 million in research and development expense and, as of December 31, 2015, had recorded current obligations of $0.6 million related to the license and service agreements with Caribou. During the year ended December 31, 2016, the Company recognized research and development expense of $1.3 million related to license and service agreements entered into with Caribou. In addition, the Company recognized general and administrative expense of $0.5 million, $0.9 million and $1.1 million during the years ended December 31, 2017, 2016 and 2015 related to the Company's obligation to pay 30.0% of Caribou's patent defense 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 9.7% of the Company's voting interests as of December 31, 2017. Refer to Note 7, *Collaborations*, for additional information regarding this collaboration agreement.

The Company recognized collaboration revenue of $9.3 million, $7.8 million and $6.0 million in the years ended December 31, 2017, 2016 and 2015, respectively, related to this agreement. As of December 31, 2017 and 2016, the Company had recorded accounts receivable of $6.0 million and $6.0 million, respectively, and deferred revenue of $11.2 million and $11.6 million, respectively, related to this collaboration.

12. Unaudited Quarterly Results

The results of operations on a quarterly basis for the years ended December 31, 2017 and 2016 are set forth below:

	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
	(Amounts in thousands except per share data)			
Collaboration revenue	$ 6,215	$ 5,917	$ 7,317	$ 6,668
Operating expenses:				
Research and development	13,431	15,565	17,481	21,170
General and administrative	5,732	6,369	5,711	10,213
Total operating expenses	19,163	21,934	23,192	31,383
Operating loss	(12,948)	(16,017)	(15,875)	(24,715)
Interest income	317	424	519	752
Net loss	$ (12,631)	$ (15,593)	$ (15,356)	$ (23,963)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.36)	$ (0.45)	$ (0.44)	$ (0.61)
Weighted average shares outstanding, basic and diluted	34,723	34,916	35,189	39,155

	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
	(Amounts in thousands except per share data)			
Collaboration revenue	$ 1,777	$ 4,206	$ 4,869	$ 5,627
Operating expenses:				
Research and development	5,225	7,423	7,861	11,331
General and administrative	3,246	3,729	4,705	5,118
Total operating expenses	8,471	11,152	12,566	16,449
Operating loss	(6,694)	(6,946)	(7,697)	(10,822)
Interest income	5	46	215	259
Net loss	$ (6,689)	$ (6,900)	$ (7,482)	$ (10,563)
Net loss per share attributable to common stockholders, basic and diluted	$ (9.89)	$ (0.36)	$ (0.22)	$ (0.31)
Weighted average shares outstanding, basic and diluted	676	19,121	34,316	34,507

EXHIBIT INDEX

Exhibit No.	Exhibit Index
3.1	Second Amended and Restated Certificate of Incorporation of the Registrant (1)
3.2	Second Amended and Restated By-laws of the Registrant (1)
4.1	Investors' Rights Agreement among the Registrant and certain of its stockholders, dated August 20, 2015 (5)
4.2	Amendment No. 1 to Investors' Rights Agreement among the Registrant and certain of its stockholders, dated April 11, 2016 (6)
4.3	Amendment No. 2 to Investors' Rights Agreement among the Registrant and certain of its stockholders, dated August 25, 2016 (3)
10.1#	2015 Amended and Restated Stock Option and Incentive Plan and forms of award agreements thereunder (3)
10.2#	Senior Executive Cash Incentive Bonus Plan (5)
10.3†	License Agreement dated as of July 16, 2014 by and between the Registrant (as successor in interest of Intellia Therapeutics, LLC) and Caribou Biosciences, Inc. (4)
10.4†	Services Agreement dated as of July 16, 2014 by and between the Registrant (as successor in interest of Intellia Therapeutics, LLC) and Caribou Biosciences, Inc. (4)
10.5†	License and Collaborative Research Agreement dated as of December 18, 2014 by and between the Registrant and Novartis Institutes for BioMedical Research, Inc. (2)
10.6#	Form of Indemnification Agreement (3)
10.7	Lease Agreement, by and between the Registrant and MIT 130 Brookline LLC, dated as of October 21, 2014 (5)
10.8	Lease Agreement, by and between the Registrant and BMR-Sidney Research Campus LLC, dated as of January 6, 2016 (5)
10.9#	2016 Employee Stock Purchase Plan (3)
10.10†	Amendment No. 1 to License Agreement dated as of February 2, 2016 by and between the Registrant and Caribou Biosciences, Inc. (5)
10.11†	Addendum to License Agreement dated as of February 2, 2016 by and between the Registrant and Caribou Biosciences, Inc. (5)
10.12†	License and Collaboration Agreement dated as of April 11, 2016 by and between the Registrant and Regeneron Pharmaceuticals, Inc. (2)
10.13	Common Stock Purchase Agreement dated as of April 26, 2016 between the Registrant and Regeneron Pharmaceuticals, Inc. (3)
10.14#	Common Stock Purchase Agreement dated as of April 26, 2016 between the Registrant and Novartis Institutes for BioMedical Research, Inc. (3)
10.15	Form of Employment Agreement for Executive Officers (3)
10.16†	Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement dated December 15, 2016 by and between the Registrant, CRISPR Therapeutics AG, The Regents of the University of California, University of Vienna, ERS Genomics Ltd., TRACR Hematology Ltd., Caribou Biosciences, Inc., and Dr. Emmanuelle Charpentier (7)

Exhibit No.	Exhibit Index
21.1	Subsidiaries of the Registrant (8)
23.1	Consent of Deloitte & Touche LLP, Independent Registered Public Accounting Firm (8)
31.1	Certification of Chief Executive Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 (8)
31.2	Certification of Chief Financial Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 (8)
32.1	Certifications pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of The Sarbanes-Oxley Act of 2002, by John M. Leonard, M.D., President and Chief Executive Officer of the Company, and Graeme Bell, Executive Vice President, Chief Financial Officer of the Company (8)
101.INS	XBRL Instance Document.
101.SCH	XBRL Taxonomy Extension Schema Document.
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.

† Application for confidential treatment of certain provisions has been granted by the Securities and Exchange Commission. Omitted material for which confidential treatment has been requested has been filed separately with the Securities and Exchange Commission.

# Indicates a management contract or any compensatory plan, contract or arrangement

(1) Incorporated by reference to the Registrant's Current Report on Form 8-K (File No. 001-37766) filed with the Securities and Exchange Commission on May 17, 2016

(2) Incorporated by reference to the Registration Statement on Form S-1 (File No. 333-210689) filed with the Securities and Exchange Commission on May 5, 2016

(3) Incorporated by reference to the Registration Statement on Form S-1 (File No. 333-210689) filed with the Securities and Exchange Commission on April 27, 2016

(4) Incorporated by reference to the Registration Statement on Form S-1 (File No. 333-210689) filed with the Securities and Exchange Commission on April 19, 2016

(5) Incorporated by reference to the Registration Statement on Form S-1 (File No. 333-210689) filed with the Securities and Exchange Commission on April 11, 2016

(6) Incorporated by reference to the Registration Statement on Form S-1 (File No. 333-210689) filed with the Securities and Exchange Commission on April 12, 2016

(7) Incorporated by reference to the Registrant's Current Report on Form 8-K (File No. 001-37766) filed with the Securities and Exchange Commission on December 16, 2016

(8) Filed with this Annual Report on Form 10-K

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

INTELLIA THERAPEUTICS, INC.

By: /s/ John M. Leonard
John M. Leonard, M.D.
President and Chief Executive Officer

Dated: March 14, 2018

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ John M. Leonard John M. Leonard, M.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 14, 2018
/s/ Graeme Bell Graeme Bell	Executive Vice President, Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 14, 2018
/s/ Caroline Dorsa Caroline Dorsa	Director	March 14, 2018
/s/ Jean François Formela Jean François Formela, M.D.	Director	March 14, 2018
/s/ Perry Karsen Perry Karsen	Director	March 14, 2018
/s/ Frank Verwiel, M.D. Frank Verwiel, M.D.	Director	March 14, 2018

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Corporate Information

EXECUTIVE OFFICERS

John M. Leonard, M.D.
Chief Executive Officer,
President

Graeme Bell
Executive Vice President,
Chief Financial Officer

José E. Rivera, J.D.
Executive Vice President,
General Counsel

BOARD OF DIRECTORS

Perry Karsen
Chairman of the Board

John M. Leonard, M.D.

Caroline Dorsa

Jean-François Formela, M.D.

Frank Verwiel, M.D.

Stockholder Information

COMPANY HEADQUARTERS
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Call U.S. Phone +1 (857) 285-6200
www.intelliatx.com

ANNUAL MEETING
The 2018 Annual Meeting of Stockholders
will be held virtually on Thursday, May 17, 2018
at 9:00am via the internet at:
www.virtualshareholdermeeting.com/NTLA2018

Intellia's common stock trades on the NASDAQ Global Market under the symbol "NTLA"

TRANSFER AGENT
Computershare Trust Company, Inc.
250 Royall Street
Canton, MA 02021
Call U.S. Phone: +1 (800) 962-4284
www.computershare.com

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