Filed Pursuant to Rule 424(b)(4)
Registration Nos. 333-210689 and 333-211176

# 6,000,000 Shares


## Common Stock

This is the initial public offering of shares of our common stock. Prior to this offering, there has been no public market for our common stock. We are selling 6,000,000 shares of our common stock. The initial public offering price of our common stock is $18.00 per share.

Our common stock has been approved for listing on The NASDAQ Global Market under the symbol "NTLA."

The underwriters have an option to purchase a maximum of 900,000 additional shares of common stock from us.

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

**Investing in our common stock involves risks. See "Risk Factors" on page 13.**

| | Price to Public | Underwriting Discounts and Commissions | Proceeds Before Expenses to Intellia Therapeutics, Inc. |
|---|---|---|---|
| Per Share | $ 18.00 | $ 1.26 | $ 16.74 |
| Total | $108,000,000 | $ 7,560,000 | $ 100,440,000 |

(1) See "Underwriting" beginning on page 151 of this prospectus for additional information regarding underwriting compensation.

Regeneron Pharmaceuticals, Inc. and Novartis Institutes for Biomedical Research, Inc., our collaboration partners, have agreed to purchase $50.0 million and $5.0 million, respectively, of our common stock in separate private placements concurrent with the completion of this offering at a price per share equal to the public offering price. The sale of such shares will not be registered under the Securities Act of 1933, as amended. The closing of this offering is not conditioned upon the closing of such concurrent private placements.

We expect that certain of our existing stockholders, including certain affiliates of our directors, will purchase an aggregate of $45.6 million of shares of our common stock in this offering at the initial public offering price.

Delivery of the shares of common stock will be made on or about May 11, 2016.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

**Credit Suisse** **Jefferies** **Leerink Partners**

**Wedbush PacGrow**

The date of this prospectus is May 5, 2016

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Through and including May 30, 2016 (25 days after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

You should rely only on the information contained in this prospectus or in any free writing prospectus we file with the Securities and Exchange Commission. Neither we nor the underwriters have authorized anyone to provide you with information other than that contained in this prospectus or any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are offering to sell, and seeking offers to buy, common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date on the front cover page of this prospectus, or other earlier date stated in this prospectus, regardless of the time of delivery of this prospectus or of any sale of our common stock.

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The market data and certain other statistical information used throughout this prospectus are based on independent industry publications, governmental publications, reports by market research firms or other independent sources that we believe to be reliable sources. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. We are responsible for all of the disclosure contained in this prospectus, and we believe these industry publications and third-party research, surveys and studies are reliable. While we are not aware of any misstatements regarding any third-party information presented in this prospectus, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties, and are subject to change based on various factors, including those discussed under the section entitled "Risk Factors" and elsewhere in this prospectus. Some data are also based on our good faith estimates.

## PROSPECTUS SUMMARY

*This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our consolidated financial statements and the related notes included elsewhere in this prospectus. You should also consider, among other things, the matters described under "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in each case appearing elsewhere in this prospectus.*

*On August 20, 2015, Intellia Therapeutics, LLC, a Delaware limited liability company, merged with and into Intellia Therapeutics, Inc., a Delaware corporation and the issuer of the shares of common stock offered by this prospectus, which we refer to as the Reorganization. As used in this prospectus, unless the context otherwise requires, references to the "Company," "Intellia," "we," "us" and "our" refer to (i) prior to the date of the Reorganization, Intellia Therapeutics, LLC and its wholly owned, consolidated subsidiary, or either or both of them as the context may require, and (ii) following the date of the Reorganization, Intellia Therapeutics, Inc.*

### Overview

We are a leading gene editing company focused on the development of proprietary, potentially curative therapeutics utilizing a recently developed biological tool known as the CRISPR/Cas9 system. We believe that the CRISPR/Cas9 technology has the potential to transform medicine by permanently editing disease-associated genes 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 gene 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 gene editing tool. Gene editing is the precise and targeted modification of the genetic material of cells. Since the publication of Dr. Doudna's landmark paper, more than 2,600 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 genes. 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. This approach has the potential to provide curative therapeutic options for patients with chronic diseases by addressing the underlying genetic cause or driver of the disease.

Unlike earlier-generation gene editing technologies, the CRISPR/Cas9 system is simple and involves a single protein, Cas9, that can be directed to precisely cleave a target DNA sequence by using pieces of RNA, called guide RNAs, that specifically recognize the target DNA of interest. Therefore, CRISPR/Cas9-based therapeutics have the potential to be highly efficient, selective and scalable.

We believe that CRISPR/Cas9 offers significant technical advantages and broader potential to edit genes over other gene editing methods. Such advantages include:

- higher selectivity and cleavage efficiency;
- simpler tools allowing for rapid scaling and optimization;
- more efficient path to achieve preclinical proof-of-concept;
- broader applicability to *in vivo* and *ex vivo* therapies;
- greater potential for single curative treatment; and
- greater potential to address polygenic or complex genetic disorders by targeting multiple DNA sites simultaneously.

We believe we are well positioned to maximize the potential of the CRISPR/Cas9 system to develop therapeutics based on the following:

- ***Strong Product Focus***. We are focused on the development of potentially curative therapeutic products through the application of the CRISPR/Cas9 system for the treatment of patient populations with significant unmet needs. We are targeting both *in vivo* and *ex vivo* applications in parallel to build a pipeline across a range of indications and to generate a wealth of data that expands the potential therapeutic applications of the CRISPR/Cas9 technology across a broad range of diseases.
- ***Deep Management Expertise in Discovering and Developing New Therapeutics.*** We have assembled a world-class team of executives, founders and advisors who are dedicated to the development of CRISPR/Cas9-based therapeutic products for patients with significant unmet medical needs. Led by Nessan Bermingham, Ph.D., our Founder and Chief Executive Officer, John M. Leonard, M.D., our Chief Medical Officer, and José E. Rivera, our Chief Operating Officer and Chief Legal Officer, our team's expertise spans CRISPR/Cas9 and broader gene editing technologies, *in vivo* and *ex vivo* therapeutic delivery technologies, preclinical and clinical development, product scale-up and manufacturing, cell and molecular biology, intellectual property, finance and regulatory affairs.
- ***Strong Product-Focused Partnerships to Accelerate Path to Clinic.*** 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 expand our impact to broader patient populations. Our partnership focusing on chimeric antigen receptor, or CAR, T cells with Novartis Institutes for BioMedical Research, Inc., or Novartis, and our partnership with Regeneron Pharmaceuticals, Inc., or Regeneron, a leader in human genetics research, exemplify this strategy.
- ***Risk-Mitigated Approach to Accelerate Product Development Path for CRISPR/Cas9 Technology.*** Our selection criteria for our initial indications position us to build a risk-diversified pipeline, where 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 initial indications to inform our selection of subsequent indications and targets of interest. We believe this approach serves to increase the probabilities of success in our initial indications, generate insights that will accelerate the development of subsequent therapeutic products and broaden the opportunity for potential strategic alliances.
- ***Delivery Expertise.*** Our team has expertise with lipid nanoparticle, or LNP, delivery technology, which involves encapsulating therapeutic agents into microscopic lipid droplets, as well as expertise with viral delivery and experience with electroporation, an electrical charge-based technique for delivering molecules into cells. With this expertise, we expect to be able to readily translate the LNPs that we are using for our preclinical development to clinical development in humans as well as continue to explore additional delivery methods.
- ***Leading Intellectual Property Position.*** Our licensed patent portfolio encompasses foundational filings on the use of CRISPR/Cas9 systems for gene editing, improvements and modifications of these systems and their components, LNP technologies for delivering protein/nucleic acid complexes and RNA into cells and cell expansion technology relevant to stem cell-based therapies. Our licensed patent portfolio also includes a United States patent application owned by The Regents of the University of California, the University of Vienna and Dr. Emmanuelle Charpentier, which is subject to an interference proceeding. Although The Regents of the University of California, the University of Vienna and Dr. Emmanuelle Charpentier have been named the senior party in the interference, meaning that they are presumed to be the earlier inventor, any adverse outcome of such proceeding may affect our ability to utilize this intellectual property.

**Our Pipeline**

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* applications, in which cells are removed from a patient's body, modified using CRISPR/Cas9 and then returned to the patient. To maximize our opportunity to rapidly develop clinically successful products, we have applied a risk-mitigated approach to selecting our initial indications, which we refer to as our sentinel indications, that have significant unmet medical needs based on four primary axes:

- 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 modalities.

We are targeting sentinel indications using *in vivo* and *ex vivo* approaches to demonstrate proof-of-concept of the various facets of our technology, including delivery, type of edit, and selectivity and efficiency. The learnings we gain from each indication will pave the way for rapid expansion of our pipeline by targeting subsequent indications that use the same or analogous delivery vehicles, guide structures and types of edits.

The following table illustrates our current discovery programs and opportunities:

| Programs | Partnerships | Type of Edit | Delivery | Upcoming Milestones |
|---|---|---|---|---|
| ***In Vivo*** | | | | |
| Transthyretin Amyloidosis (ATTR) | Co-developing with Regeneron | Knockout | LNP to Liver | Select 1 to 2 development candidates and advance to IND enabling studies in the next 12 to 24 months |
| Alpha-1 Antitrypsin Deficiency (AATD) | Proprietary | Knockout Repair | LNP to Liver | |
| Hepatitis B Virus (HBV) | Proprietary | Knockout | LNP to Liver | |
| Inborn Errors of Metabolism (IEMs) | Proprietary | Knockout Repair Insertion | LNP to Liver | |
| ***Ex Vivo*** | | | | |
| Hematopoietic Stem Cells (HSCs) | Selectively partnered with Novartis; proprietary | Knockout Repair Insertion | Electroporation | First Novartis IND expected to be submitted in 2018 |
| CAR T Cells | Partnered with Novartis | Knockout Insertion | Electroporation | Advance preclinical development |

**In Vivo *Pipeline***

We have chosen four sentinel *in vivo* liver programs employing different editing strategies to explore the scope of the gene edits through the CRISPR/Cas9 system:

- Transthyretin amyloidosis, or ATTR, program, which utilizes a gene knockout strategy;
- Alpha-1 antitrypsin deficiency, or AATD, program, which utilizes either a gene knockout strategy or a gene repair strategy;
- Hepatitis B virus, or HBV, program, which utilizes a knockout strategy to target covalently closed circular DNA, or cccDNA; and

- Inborn errors of metabolism, or IEM, program, which has the potential to utilize all three editing approaches, including targeted DNA insertion.

Our initial efforts on *in vivo* delivery approaches focus on the use LNPs for delivery of the CRISPR/Cas9 complex to the liver. We see multiple advantages of using LNPs as our initial *in vivo* delivery vehicles, particularly as being optimized by us for delivery of the CRISPR/Cas9 system. Certain LNPs have demonstrated efficacy, safety and favorable tolerability and are currently used as a delivery system for therapeutic small interfering RNA, or siRNA, as well as therapeutic messenger RNA, or mRNA. mRNA is RNA that encodes proteins, while siRNA is RNA that can interfere with the function of mRNA. With our team's expertise with LNP delivery technology, we expect to be able to readily translate the LNPs that we are using for our preclinical development to clinical development in humans. As we progress our sentinel *in vivo* liver programs with LNP delivery, we are actively investigating additional delivery methods, including evaluating multiple viral delivery vectors, which are viruses engineered to carry non-viral nucleic acids to patients' cells. These additional or enhanced delivery methods may assist us in exploring therapies for indications that require delivery to organs beyond the liver.

*Transthyretin Amyloidosis Program (Knockout Strategy)*

ATTR is a disorder caused by certain genetic mutations that can cause the transthyretin, or TTR, protein to aggregate and accumulate in tissues. Accumulation of this protein in peripheral nerves or the heart can result in a severe loss of nerve or cardiac function. Estimates suggest that approximately 50,000 patients suffer from ATTR worldwide. We believe that we can apply the CRISPR/Cas9 technology to potentially cure ATTR by knocking out expression of the defective *TTR* gene in the liver, reducing or eliminating the production of the disease-causing mutant form of the TTR protein.

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

AATD is an inherited genetic disorder that may cause lung or liver disease. The lung disease may result in chronic obstructive pulmonary disease, or COPD, a progressive disease that causes substantial morbidity and mortality, while the liver disease is characterized by inflammation of the liver. In the United States, an estimated 60,000 to 100,000 people have AATD, which arises when patients have a mutation in both copies of the *SERPINA1* gene. We believe that we can apply the CRISPR/Cas9 technology to potentially cure AATD by addressing the defective *SERPINA1* gene. We intend to evaluate two editing approaches – a knockout and a repair – which will address either the liver disease or both the lung and liver diseases, respectively. We expect the progress of our AATD repair program to follow our AATD knockout program.

*Hepatitis B Virus Program (Knockout Strategy)*

Hepatitis B is an infection of the liver caused by HBV, which can progress from acute to chronic infection in approximately 5-10% of infected adults. We believe we can use the CRISPR/Cas9 system to help eliminate the reservoirs of cccDNA, the source of chronic infection, which cannot be eradicated by current treatments, in HBV-infected patients. We intend to evaluate different knockout approaches to destroy or render inactive cccDNA *in vivo*, including cleaving the cccDNA at a single site or at combinations of sites. We believe it is also possible that a common treatment solution can be developed for all genotypes, or genetic variants, of HBV because we can target portions of the cccDNA sequences that do not vary across genotypes. In addition, there is potential to reduce viral resistance as the virus itself is eradicated. We have completed a bioinformatics analysis of potential CRISPR/Cas9 target sites in the HBV genome to select a set of guide RNAs, including several that can be effective across all HBV genotypes.

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

Individual IEMs are rare disorders, many having an incidence of fewer than 1 in 100,000 births, which typically involve defects in single genes that code for enzymes that drive the metabolic machinery of the cell. We

are evaluating a large set of candidate IEMs, including primary hyperoxaluria type 1, or PH1, argininosuccinic lyase deficiency, ornithine transcarbamylase deficiency, phenylketonuria, or PKU, and maple syrup urine disease. Our selection criteria for our initial 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.

**Ex Vivo *Pipeline***

Our sentinel *ex vivo* programs are in CAR T cell and hematopoietic stem cell, or HSC, applications. Our sentinel *ex vivo* programs will help inform the broader applicability of CRISPR/Cas9 in an *ex vivo* setting, which we plan to explore in eXtellia, a division of our company focused on the application of CRISPR/Cas9 gene editing in the fields of immuno-oncology and autoimmune and inflammatory diseases. We expect eXtellia to focus on other relevant types of immune cells, such as natural killer, or NK cells, and tumor infiltrating lymphocytes, or TILs, for immuno-oncology applications, T regulatory cells, or Tregs, for autoimmune disorders and other cell types, including induced pluripotent stem cells, mesenchymal stem cells and muscle satellite stem cells for tissue-targeted treatments. For our *ex vivo* programs requiring delivery to extracted cells such as HSCs, which are the stem cells from which all of the various types of blood cells originate, or T cells, we initially plan to deliver the CRISPR/Cas9 complex by electroporation, an electrical charge-based technique for delivering molecules into cells. In parallel with electroporation, we are considering several newer technologies for delivery to cells *ex vivo*, which may provide advantages in delivery efficiency or cell viability.

*CAR T Cell Program*

In CAR T cell therapy, naturally occurring immune cells, specifically T cells, are modified *ex vivo* by inserting a chimeric antigen receptor, or CAR, to selectively target cancer cells and activate an immune response against them. The CAR is an engineered fusion protein expressed on a cell's surface that has an antibody-based portion capable of recognizing certain markers on other cells, such as cancer cells, and a signaling portion inside the cell capable of delivering 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 immune checkpoint pathways.

*HSC Program*

For our HSC programs, we intend to apply CRISPR/Cas9 to correct defective proteins in HSCs of a given patient for the potential treatment of blood disorders or primary immune deficiencies. Challenges of developing stem cell products 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 by employing a proprietary small molecule for HSC expansion to which Novartis has granted us rights. This compound could allow us to generate large numbers of HSCs for re-implantation in patients after editing. We are also pursuing a number of potential gene targets and therapeutic indications in collaboration with Novartis. 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. We expect the first investigational new drug application for an HSC program under the Novartis collaboration to be submitted by Novartis in 2018.

Ex Vivo *Collaboration*

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. Under this collaboration agreement, we received an upfront technology access payment of $10.0 million and are entitled to up to an additional $40.0 million, in aggregate, in additional technology access fees and research payments during the five-year collaboration term. 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.

**Strategy**

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

- focus on sentinel indications that enable us to fully develop the potential of the CRISPR/Cas9 system;
- aggressively pursue *in vivo* liver indications to develop therapeutics rapidly with existing delivery technology;
- continue to develop and expand our *ex vivo* therapeutic programs through our eXtellia division;
- continue to leverage strategic partnerships to accelerate clinical development; and
- grow our leadership position in the field of gene editing.

**Series B Financing**

To enable further development of our technology and *in vivo* and *ex vivo* programs, we completed a private placement for gross proceeds of $70.0 million of our Series B preferred stock in August 2015 led by OrbiMed Advisors LLC. Additional investors in this financing included Fidelity Management & Research, Janus Capital Management, Foresite Capital, Sectoral Asset Management, EcoR1 Capital LLC, our existing investors, Atlas Venture Fund IX, LP and Novartis, as well as other leading mutual fund and healthcare investors.

**Risks Associated With Our Business**

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the section entitled "Risk Factors" appearing immediately following this prospectus summary. These risks include the following:

- CRISPR/Cas9 gene editing technology is a novel technology that is not yet proven or clinically validated for human therapeutic use. 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.
- 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 and clinical studies from the U.S. Food and Drug Administration and other regulatory authorities, before we can seek regulatory approval and begin commercial sales of any potential product candidates.
- Negative public opinion and increased regulatory scrutiny of gene editing therapies may damage public perception of the safety of any product candidates that we develop and adversely affect our ability to conduct clinical trials or obtain regulatory approvals for such product candidates.
- Third-party claims of intellectual property infringement against us, our licensors or our collaborators may prevent or delay our product discovery and development efforts.
- We license a patent family under our license agreement with Caribou Biosciences, Inc. that covers CRISPR/Cas9 systems and methods to edit genes. A United States patent application in this patent family is subject to an interference proceeding, the outcome of which may adversely affect our ability to utilize this intellectual property.
- We may not be successful in our efforts to use and enhance our gene editing technology to create a pipeline of product candidates and develop commercially successful products, or we may expend our limited resources on programs that do not yield a successful product candidate.

- We face significant competition in an environment of rapid technological change. We are aware of at least three other CRISPR/Cas companies and five gene editing companies with platforms other than CRISPR/Cas. The possibility that one or more of our competitors may develop therapies that are more effective than ours or achieve regulatory approval before us may harm our business and financial condition.
- We have never generated any revenue from product sales, do not expect to do so in the near term and may never achieve or maintain profitability. We expect to incur losses for the foreseeable future and will need to raise substantial additional funding, even with the net proceeds expected from this offering and the concurrent private placements.
- We have entered into, and may in the future enter into, collaborations with third parties to develop product candidates. If these collaborations are not successful, our business could be adversely affected.

**Implications of Being an Emerging Growth Company**

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure about our executive compensation arrangements;
- no non-binding advisory votes on executive compensation or golden parachute arrangements; and
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or SEC. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. We have irrevocably elected to ''opt out'' of the exemption for the delayed adoption of certain accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

**Concurrent Private Placements**

Regeneron and Novartis, our collaboration partners, have agreed to purchase $50.0 million and $5.0 million, respectively, of our common stock in separate concurrent private placements at a price per share equal to the public offering price. The sale of such shares will not be registered under the Securities Act of 1933, as amended. The closing of this offering is not conditioned upon the closing of such concurrent private placements.

**Corporate History**

We were incorporated under the laws of the State of Delaware in May 2014. We are the successor in interest to Intellia Therapeutics, LLC, a limited liability company formed under the laws of the State of Delaware in

July 2014 and the former holder of all of our outstanding shares of stock. Our principal executive office is located at 130 Brookline Street, Suite 201, Cambridge, MA 02139, and our telephone number is (857) 285-6200. Our website address is www.intelliatx.com. We do not incorporate the information on or accessible through our website into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus.

We own various U.S. federal trademark applications and unregistered trademarks, including our company name. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the symbols ® and ™, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

**Reorganization**

As more fully described in the section entitled "Reorganization" appearing elsewhere in this prospectus, on August 20, 2015, we completed a series of transactions pursuant to which Intellia Therapeutics, LLC merged with and into Intellia Therapeutics, Inc., with Intellia Therapeutics, Inc. continuing as the surviving corporation. In connection with this 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 OFFERING**

| | |
|---|---|
| Common stock offered in this offering | 6,000,000 shares |
| Common stock to be sold to Regeneron and Novartis in the concurrent private placements | 3,055,554 shares |
| Common stock to be outstanding immediately after this offering and the concurrent private placements | 35,096,265 shares (35,996,265 shares if the underwriters exercise their option to purchase additional shares in full) |
| Underwriters' option to purchase additional shares | We have granted a 30-day option to the underwriters to purchase up to an aggregate of 900,000 additional shares of common stock from us at the public offering price, less underwriting discounts and commissions on the same terms as set forth in this prospectus. |
| Use of proceeds | We estimate that we will receive net proceeds from the sale of shares of our common stock in this offering of approximately $97.8 million, or $112.9 million if the underwriters exercise their option to purchase additional shares in full, based on the initial public offering price of $18.00 per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering to advance the research and development of our sentinel indications, progress additional *in vivo* and *ex vivo* pipeline product candidates, further develop our delivery technologies and CRISPR/Cas9 gene editing platform and for working capital and other general corporate purposes. For a more complete description of our intended use of the proceeds from this offering, see "Use of Proceeds." |
| Risk factors | You should carefully read the "Risk Factors" section of this prospectus for a discussion of factors that you should consider before deciding to invest in our common stock. |
| NASDAQ Global Market symbol | "NTLA" |

We expect that certain of our existing stockholders, including certain affiliates of our directors, will purchase an aggregate of $45.6 million of shares of our common stock in this offering at the initial public offering price.

The number of shares of our common stock to be outstanding after this offering and the concurrent private placements is based on 26,040,711 shares of our common stock outstanding as of March 31, 2016, including 23,481,956 shares of our common stock issuable upon the automatic conversion of all outstanding shares of our preferred stock upon the closing of this offering, and excludes:

- 496,539 shares of common stock reserved for future issuance as of March 31, 2016 under our 2015 Stock Option and Incentive Plan, or the 2015 Plan, which was amended and restated as our 2015 Amended and Restated Stock Option and Incentive Plan, or the 2015 Restated Plan, in connection with the effectiveness of the registration statement of which this prospectus is a part;

- 2,617,932 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2016, at a weighted average exercise price of $6.69 per share; and
- an additional 2,001,579 shares of common stock that will be made available for future issuance under our equity compensation plans upon the closing of this offering.

Unless otherwise indicated, all information in this prospectus gives effect to the Reorganization described in the section entitled "Reorganization" and reflects or assumes the following:

- the filing of our amended and restated certificate of incorporation upon the closing of this offering and the effectiveness of our amended and restated by-laws upon the effectiveness of the registration statement of which this prospectus is a part;
- the conversion of all of our outstanding shares of preferred stock into an aggregate of 23,481,956 shares of common stock upon the completion of this offering; and
- no exercise by the underwriters of their option to purchase up to 900,000 additional shares of common stock in this offering.

In addition, unless otherwise indicated all information in this prospectus gives effect to a one-for-1.7 reverse stock split of our common stock that was effected on April 25, 2016.

## SUMMARY CONSOLIDATED FINANCIAL DATA

The summary consolidated financial data set forth below should be read together with the consolidated financial statements and the related notes to those statements, as well as the sections entitled "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." We have derived the summary consolidated statement of operations data for the period from May 7, 2014 (inception) to December 31, 2014 and for the year ended December 31, 2015 and the summary consolidated balance sheet data as of December 31, 2015 from our audited consolidated financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of results that may be expected in the future.

| | Period from May 7, 2014 (inception) to December 31, 2014 | Year Ended December 31, 2015 |
|---|---|---|
| | (in thousands, except per unit and per share data) | |
| Collaboration revenue | $ — | $ 6,044 |
| Operating expenses: | | |
| Research and development | 1,105 | 11,170 |
| In-process research and development | 6,055 | — |
| General and administrative | 2,379 | 8,283 |
| Total operating expenses | 9,539 | 19,453 |
| Loss before income taxes | (9,539) | (13,409) |
| Benefit from income taxes | — | 1,012 |
| Net loss | $ (9,539) | $ (12,397) |
| Net loss per common unit, basic and diluted | $ (11.55) | $ — |
| Net loss per share attributable to common stockholders, basic and diluted | $ — | $ (51.02) |
| Weighted average common units outstanding, basic and diluted | 826 | — |
| Weighted average shares outstanding, basic and diluted | — | 243 |
| Pro forma net loss per share, basic and diluted (unaudited)(1) | | $ (0.70) |
| Pro forma weighted average shares outstanding, basic and diluted (unaudited)(1) | | 17,664 |

| | As of December 31, 2015 | | |
|---|---|---|---|
| | Actual | Pro Forma(2) | Pro Forma As Adjusted(3) |
| | (in thousands) | | |
| **Consolidated Balance Sheet Data:** | | | |
| Cash and cash equivalents | $ 75,816 | $ 75,816 | $ 228,656 |
| Working capital(4) | 66,931 | 66,931 | 219,771 |
| Total assets | 82,139 | 82,139 | 234,979 |
| Deferred revenue | 10,312 | 10,312 | 10,312 |
| Convertible preferred stock | 88,557 | — | — |
| Total stockholders' (deficit) equity | (21,201) | 67,356 | 220,196 |

(1) Basic and diluted pro forma net loss per share give effect to the conversion of all shares of preferred stock issued in connection with the Reorganization into shares of common stock immediately prior to the completion of this offering, assuming such conversion occurred on the later of May 7, 2014 (inception) or the issuance date of the corresponding unit that converted to preferred stock in the Reorganization.

(2) Pro forma amounts give effect to the automatic conversion of all of our outstanding shares of preferred stock into an aggregate of 23,481,956 shares of common stock upon the completion of this offering.

(3) Pro forma as adjusted amounts reflect pro forma adjustments described in footnote (2) as well as (i) the sale of 6,000,000 shares of our common stock in this offering at the initial public offering price of $18.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us and (ii) our sale of $55.0 million of our common stock in concurrent private placements to Regeneron and Novartis at the initial public offering price of $18.00 per share. Pro forma as adjusted amounts do not include a $75.0 million upfront payment received from Regeneron in April 2016 under our license and collaboration agreement.

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

## RISK FACTORS

*Investing in our common stock involves a high degree of risk. You should carefully consider the following risks and uncertainties, together with all other information in this prospectus, including our consolidated financial statements and related notes and "Management's Discussion and Analysis of Results of Operations and Financial Condition," before investing in our common stock. Any of the risk factors we describe below could adversely affect our business, financial condition or results of operations. The market price of our common stock could decline if one or more of these risks or uncertainties actually occur, causing you to lose all or part of the money you paid to buy our common stock. Additional risks that we currently do not know about or that we currently believe to be immaterial may also impair our business. Certain statements below are forward-looking statements. See "Cautionary Note Regarding Forward-Looking Statements" in this prospectus.*

### Risks Related to Our Business, Technology and Industry

***CRISPR/Cas9 gene editing technology is a novel technology that 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 potentially curative medicines utilizing the CRISPR/Cas9 gene editing technology. Although there have been significant advances in the field of gene therapy, which typically involves introducing a copy of a gene into a patient's cell, and gene editing in recent years, CRISPR-based gene editing technologies are new and largely unproven. The CRISPR/Cas9 technologies that we have licensed and that we intend to develop have not yet been clinically tested by us, nor are we 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 safely delivering a therapeutic into target cells safely within the human body or in an *ex vivo* setting, optimizing the efficiency and specificity of such products, and ensuring the therapeutic selectivity of such products. There can be no assurance we will be successful in solving any or all of these issues.

We have concentrated our research efforts to date on bringing CRISPR/Cas9 therapeutics to the clinic for our initial indications, which we call our sentinel indications, and our future success is highly dependent on the successful development of CRISPR-based gene editing technologies, cellular delivery methods and therapeutic applications. Our sentinel indications are the 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 sentinel indications or any other indication we pursue.

Public perception and related media coverage of potential therapy-related safety issues, including adoption of new therapeutics or novel approaches to treatment, as well as ethical concerns related specifically to gene editing and CRISPR/Cas9, may adversely influence the willingness of subjects to participate in clinical trials, or if any therapeutic is approved, of physicians to subscribe to the novel treatment mechanics. Physicians, hospitals and third-party payors often are slow to adopt new products, technologies and treatment practices that require additional upfront costs and training. Physicians may not be willing to undergo training to adopt this novel and personalized therapy, may decide the therapy is too complex to adopt without appropriate training and may choose not to administer the therapy. 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. Based on these and other factors, hospitals and payors may decide that the benefits of this new therapy do not or will not outweigh its costs.

Development activities in the field of CRISPR/Cas9 are currently subject to a number of risks related to the ownership and use of certain intellectual property rights that are subject to patent interference proceedings. 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 prospectus for more information.

***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-based and viral diseases centers on using the CRISPR/Cas9 technology to introduce or remove genetic information in order to treat various disorders. Because this is a new therapeutic approach, discovering, developing and commercializing our product candidates subject us to a number of challenges, including:

- obtaining regulatory approval from the U.S. Food and Drug Administration, or 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 guidance regarding potential regulatory pathways for this category of therapeutics, including preclinical and clinical requirements for approval of an investigational new drug application, or 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 after obtaining any regulatory approval to gain market acceptance.

Additionally, because our 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 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 genetic modification of patient cells have been approved in the United States and only one has been approved in the European Union, or EU;
- improper insertion of a gene sequence into a patient's chromosome could lead to lymphoma, leukemia or other cancers, or other aberrantly functioning cells;

- 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 genetically modified cells conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health, or the NIH, are subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or 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.

To date, neither we nor any other company has received regulatory approval to commence human clinical trials or to market therapeutics utilizing CRISPR/Cas9. The regulatory pathway for therapeutics such as those we are developing is unclear and the FDA and other regulatory authorities have not yet provided written guidance regarding preclinical or clinical studies or regulatory approval pathways for gene editing 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 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.

***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 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 prevalence and severity of any side effects;
- 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 as well as competitive products;
- the cost of treatment in relation to alternative treatments;
- the amount of upfront costs or training required for physicians 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 use of CRISPR/Cas9 or other therapeutics mediums such as viral vectors that we anticipate using in our clinical trials may limit market acceptance of our product candidates. If our product candidates are approved but fail to achieve market acceptance among physicians, patients, hospitals, third-party payors or others in the medical community, we will not be able to generate significant revenue.

***Negative public opinion and increased regulatory scrutiny of CRISPR/Cas9, 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 no gene therapy product approved to date in the United States and only one gene therapy product approved to date in the EU. Public perception may be influenced by claims that gene therapy or gene editing, including through 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. 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. 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 United States, 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 United States 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 United States 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 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 do not currently have any product candidates. 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 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 beyond the net proceeds of this offering and concurrent private placements 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;
- we may not be able or willing to assemble sufficient resources to acquire or discover product candidates;
- our product candidates may not succeed in preclinical or clinical testing;
- our planned risk mitigation strategy for selecting our sentinel 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 products candidates;
- our therapeutic delivery systems may fail so that even a product candidate with therapeutic activity does not demonstrate a clinically meaningful therapeutic effect;
- a product candidate may not demonstrate in patients the biological, chemical and pharmacological properties identified in laboratory 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; 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 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 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 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 focus on research programs that we identify as our sentinel indications. As a result, we may fail to capitalize on 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 exclusive 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.

***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 stage, and their risk of failure is high. It is impossible to predict when or if any of our programs will prove effective and safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of any of our future product candidates in humans. Preclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. We may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful, and a clinical trial can fail at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

Successful completion of clinical trials is a prerequisite to submitting a biologics license application, or BLA, to the FDA, a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA and similar approval 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 that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards, or 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, or 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 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 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, or 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, 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, 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, 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 withdraw their written guidance, if any, regarding the applicable regulatory approval pathway or any approval of the product in question, or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy, or 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 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 factors.***

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 some time 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 factors, including:

- selecting commercially viable product candidates and effective delivery methods;
- completing research and nonclinical 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 patent 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;

- 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.

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, 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:

- gene editing companies focused on CRISPR/Cas9 including: CRISPR Therapeutics, Inc., Editas Medicine, Inc. and Tracr Hematology Limited;
- other gene editing companies including: bluebird bio, Inc., Cellectis S.A., Poseida, Inc., Precision BioSciences, Inc. and Sangamo BioSciences; and
- gene therapy companies developing *ex vivo* therapies including: bluebird bio, Inc., Cellectis S.A., and Juno Therapeutics, Inc.

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

In addition, certain of our founders previously have had, and may in the future have, affiliations with other gene editing companies.

Any advances in gene therapy 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, 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 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 United States.

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 our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment.

***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 will 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. For the period from May 7, 2014 (inception) to December 31, 2014, we reported a net loss of $9.5 million. For the year ended December 31, 2015, we reported a net loss of $12.4 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 will need to raise substantial additional funding, even with the net proceeds expected from this offering and concurrent private placements. 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. We expect to spend substantial amounts of our financial resources on our discovery programs going forward. If we are able to identity 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.

As of December 31, 2015, we had $75.8 million in cash and cash equivalents. We estimate that our net proceeds from this offering and the concurrent private placements will be approximately $152.8 million, based on the initial public offering price of $18.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We expect to use the net proceeds from this offering to advance the research and development of our sentinel indications, to progress additional pipeline product candidates, to further develop our delivery technologies and CRISPR/Cas9 gene editing platform and for working capital and other general corporate purposes. We believe that such proceeds, together with our existing cash, revenue under our collaborations with Novartis Institutes for BioMedical Research, Inc., or Novartis, and Regeneron Pharmaceuticals, Inc., or Regeneron, including a $75.0 million upfront payment received from Regeneron, and the proceeds from our concurrent private placements will be sufficient to fund our operations for at least the next 36 months. However, changing circumstances may cause us to increase our spending significantly faster than we currently anticipate, and we may need to spend more money than currently expected. In this regard, 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, including purchasers of common stock in this offering, 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, your ownership interest may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. 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 United States. If patients are unwilling to participate in our clinical studies because of 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 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 our 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 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 product development, regulatory affairs and, if any product candidates 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 and business development expertise of Nessan Bermingham, Ph.D., our President and Chief Executive Officer, John M. Leonard, M.D., our Chief Medical Officer and José E. Rivera, our Chief Operating Officer and Chief Legal Officer as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment arrangements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be important for our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products using our technology. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies, universities and research institutions for similar personnel. The market for qualified personnel in the biotechnology space generally, and 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. 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 and marketing capabilities or enter into agreements with third parties to sell and market 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 or marketing 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 and when 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; and
- unforeseen costs and expenses associated with creating an independent 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 chimeric antigen receptor T cells, or CAR T cells, and hematopoietic stem cells, or HSCs. Under the Novartis collaboration agreement, we received an upfront commitment to advance multiple programs. Pursuant to the Novartis agreement, we granted Novartis exclusive rights to further develop any products arising out of the CAR T cell program. Regarding HSCs, we plan to jointly advance multiple programs with Novartis and have agreed to a process for assigning development and ownership rights, which will 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 sentinel indications, other than ATTR, which is 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 under collaboration with other companies, including some of our competitors, and Novartis's or Regeneron's own corporate objectives 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 would 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 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 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 independently develop, or develop 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 commercialization of our product candidates;
- collaborators may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- collaborators with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional 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 our 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;
- 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, 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 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 development, regulatory approval and commercialization described in this prospectus 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 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 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 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 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 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 product candidates 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 contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error 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 biologic such as ours generally cannot be fully characterized. As a result, assays of the finished product 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 or insufficient inventory. 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 or product recalls. Lot failures or product recalls 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 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.***

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 and 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 do not control the manufacturing process of, and will be completely dependent on, our contract manufacturing partners for compliance with regulatory requirements, known as good manufacturing practice, or cGMP, requirements for manufacture 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 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. 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 regulatory 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 biologic product produced under current good manufacturing practice, or cGMP, requirements and may require a large number of test patients.

Our failure or any failure by these third parties to comply with these regulations 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 federal or state fraud and abuse or false claims laws and regulations or healthcare 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 or not 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, there is a natural transition period when a new CRO begins work. As a result, delays may occur, 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 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, recent global financial crises caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, 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 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, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or 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 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 United States, 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 United States and other regulatory authorities. We are not permitted to market any biological product in the United States until we receive a biologics license from the FDA. We have not previously submitted a BLA to the FDA, or similar approval filings to comparable foreign authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe, pure and potent for each desired indication. The BLA must also include significant information regarding the chemistry, manufacturing and controls for the product, and the manufacturing facilities must complete a successful pre-license inspection. We expect the novel nature of our product candidates to create further challenges in obtaining regulatory approval. For example, the FDA has no experience with commercial development of CRISPR/Cas9-based therapies for human therapeutic use. The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain approval of any product candidates that we develop based on the completed clinical trials. Moreover, while we are not aware of any specific genetic or biomarker diagnostic tests for which regulatory approval would be necessary in order to advance any of our product candidates to clinical trials or potential commercialization, in the future regulatory agencies may require the development and approval of such tests. Accordingly, the regulatory approval pathway for such product candidates may be uncertain, complex, expensive and lengthy, and approval may not be obtained.

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

- obtaining regulatory authorization to begin 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 delayed. 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 United States, 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 United States, 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, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMP and GCP 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, current Good Tissue Practices, or cGTP, regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any BLA, other marketing application, 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 requirements including submissions of safety and other post-marketing information and reports and registration.

The FDA may 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 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 United States 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 compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

***Healthcare cost control initiatives, including healthcare legislative 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 United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In particular, there have been and continue to be a number of legislative initiatives at the United States federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the Affordable Care Act, was enacted, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts 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.

In addition, other legislative changes have been proposed and adopted in the United States 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. These new laws may result in additional reductions in Medicare, Medicaid and other healthcare funding, which could have a material adverse effect on our 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. We cannot predict the initiatives that may be adopted in the future, any of which could limit the amounts that foreign, federal and state governments 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 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 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 United States and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, 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 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 and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.***

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our 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 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 United States 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, through civil whistleblower or *qui tam* actions, 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, or 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; and
- the Federal Food, Drug and Cosmetic Act, which prohibits, among other things, the adulteration or misbranding of drugs and medical devices.

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 narrowness of the 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.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations 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 United States 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 laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.***

We will become subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations will involve 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 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 patents and proprietary rights of third parties. There is a substantial amount of litigation, as well as administrative proceedings for challenging patents, including interference, derivation, and reexamination proceedings before the United States Patent and Trademark Office, or 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. Recently, due to changes in U.S. law referred to as patent reform, new procedures including *inter partes* review and post-grant review have been implemented. This reform adds uncertainty to the possibility of challenge to our developed or licensed patents in the future.

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 the biotechnology and pharmaceutical industries expand 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.

Third parties may assert that we infringe their patents or that we are otherwise employing their proprietary technology without authorization, and may sue us. These third parties could include the co-owners of patent families that we license and from whom we have not yet obtained consent to practice the intellectual property in countries outside the United States, such as the co-owners of the intellectual property owned by The Regents of the University of California and the University of Vienna, which we refer to collectively as UC/Vienna, and Dr. Emmanuelle Charpentier from whom we do not yet have a license. 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 asserting their patent rights against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. For example, the Broad Institute, Inc., or the Broad Institute, the Massachusetts Institute of Technology, or MIT, and the President and Fellows of Harvard College, or Harvard, own a patent portfolio, collectively, the Broad

Institute patent family, including issued patents in the U.S. and Europe, that purports to cover certain aspects of the CRISPR/Cas9 gene editing platform for use on gene sequences from eukaryotic cells, including human cells. An interference proceeding has been declared in the USPTO between certain U.S. patents and one application of the Broad Institute patent family and one UC/Vienna and Dr. Charpentier patent application we license through Caribou Biosciences Inc., or Caribou, which means that the USPTO will determine whether the contested inventions belong either to UC/Vienna and Dr. Charpentier or to the Broad Institute. While the UC/Vienna/Charpentier group has been named the senior party in the interference, meaning that they are presumed to be the earlier inventor, it is possible that the Broad Institute patent family will be upheld by the USPTO and could be asserted against us during development or commercialization of one of our CRISPR/Cas9-based products. 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 would be unable to further develop and commercialize our product candidates, which could harm our business significantly.

If we are found to infringe a third party's 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 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 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, with respect to the matter involving the Broad Institute patent family mentioned above, 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.

***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. One United States patent application in this patent family is subject to interference proceedings with certain patents and a patent application of the Broad Institute patent family. The outcome of these proceedings 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 gene sequences from eukaryotic cells, including human cells. On January 11, 2016, the Patent Trial and Appeal Board of the USPTO, or PTAB, declared an interference proceeding between certain patents and a patent application of the Broad Institute patent family and one UC/Vienna and Dr. Charpentier patent application to determine, based on priority of invention, whether the contested inventions belong either to UC/Vienna and Dr. Charpentier or to the Broad Institute. The UC/Vienna/Charpentier group has been named the senior party in the interference and is therefore presumed to be the earlier inventor. As the junior party in the proceeding, the Broad Institute bears the burden of proof to support its claim that it was the first to invent the claimed patents. If the Broad Institute is able to ultimately prevail in the proceedings, its patents could be asserted against us during development or commercialization of one of our CRISPR/Cas9-based products. 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.

***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 University of California, Berkeley 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, co-owners from whom we do not yet have a license may raise claims surrounding inventorship or ownership of patents that ultimately issue from this patent family, potentially resulting in issued patents to which we would not have rights under our existing license. Further, in jurisdictions outside the United States, a license may not be enforceable unless all the owners of the intellectual property agree or consent to the license. Accordingly, Dr. Charpentier could seek monetary or equitable relief requiring us to pay her compensation for, or refrain from, exploiting these patents due to the co-ownership of the UC/Vienna intellectual property we license through Caribou. In addition, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation 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 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, 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. See the section entitled “Business—Intellectual Property” for additional information regarding our license agreements.

Disputes may also 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 and processes infringe on 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;
- 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 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 of the licensed patents and our licensors’ overall patent enforcement 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. 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 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 have been or will be conducted in compliance with applicable laws and regulations 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, and in some cases, their 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. Even if we are not a party to these legal actions, 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 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 or delivery systems that may require the use of additional proprietary rights held by third parties. Our ultimate product candidates may also require specific formulations to work effectively and efficiently. These 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. If we are unable to successfully obtain rights to required 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.

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.

***We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products or product candidates.***

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

- if and when any patents will issue;
- the 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; or
- whether we will need to initiate litigation or administrative proceedings to 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 United States 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 United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability, or scope thereof, which may result in such patents being narrowed, invalidated, or held unenforceable. 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 United States 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. 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. For U.S. applications containing a claim not entitled to priority before March 16, 2013, there is a greater level of uncertainty in the patent law in view of the passage of the America Invents Act, which brought into effect significant changes to the U.S. patent laws, including new procedures for challenging pending patent applications and issued patents.

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 United States and abroad.

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 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.

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 United States 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 United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States 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.

As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. 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 United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

***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 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 United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States 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 United States. 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 United States can have a different scope and strength than do those in the United States. 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 United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States 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 United States. 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. Further, in jurisdictions outside the United States, a license may not be enforceable unless all the owners of the intellectual property agree or consent to the license.

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. 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 United States, 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 United States 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. 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 Caribou and Novartis 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, than 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 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 and this Offering**

***We expect that our stock price will fluctuate significantly and investors may not be able to resell their shares at or above the initial public offering price.***

The trading price of our common stock following this offering may be highly volatile and could be subject to wide fluctuations in response to various factors, many of which are beyond our control. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the initial public offering price. The market price for our common stock may be influenced by many factors, including those discussed in this "Risk Factors" section and elsewhere in this prospectus and the following:

- the results of our efforts to discover, develop, acquire or in-license product candidates;
- success of competitive products or technologies;
- results or delays in clinical trials or changes in the development status of our future product candidates;
- any delay in our regulatory filings for any product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings;
- regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to our products, including clinical trial requirements for approvals;

- our inability to obtain or delays in obtaining adequate product supply for any approved product or inability to do so at acceptable prices;
- any failure to commercialize any product candidates or if the size and growth of the markets we intend to target fail to meet expectations;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to CRISPR/Cas9-based therapy or the use of our and competitors' product candidates;
- introductions or announcements of new products offered by us or significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our collaborators or our competitors and the timing of such introductions or announcements;
- our ability to effectively manage our growth;
- our ability to successfully treat additional types of genetic-based diseases;
- changes in the structure of healthcare payment systems;
- actual or anticipated changes in estimates to or projections of financial results, development timelines or recommendations by securities analysts;
- publication of research reports about us or our industry, or gene editing in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- market conditions in the pharmaceutical and biotechnology sectors or the economy generally;
- our ability or inability to raise additional capital through the issuance of equity or debt or collaboration arrangements and the terms on which we raise it;
- trading volume of our common stock;
- disputes or other developments relating to proprietary rights, including patents, litigation or interference matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation; and
- general economic, industry and market conditions.

The stock market in general, and market prices for the securities of biopharmaceutical companies like ours in particular, have from time to time experienced volatility that often has been unrelated to the operating performance of the underlying companies. These broad market and industry fluctuations may adversely affect the market price of our common stock, regardless of our operating performance. In several recent situations when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit against us, the defense and disposition of the lawsuit could be costly and divert the time and attention of our management and harm our operating results.

***An active trading market for our common stock may not develop.***

Prior to this offering, there has been no public market for our common stock and an active trading market for our shares may never develop or be sustained following this offering. The initial price to the public for our common stock was determined through negotiations with the underwriters, and the negotiated price may not be indicative of the market price of the common stock after the offering. The lack of an active market may impair investors' ability to sell their shares at the time they wish to sell them or at a price that they consider reasonable, may reduce the market value of their shares and may impair our ability to raise capital.

***If securities or industry analysts do not publish research reports about our business, or if they issue an adverse opinion about our business, our stock price and trading volume could decline.***

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not currently have and may never obtain research coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, or one or more of the analysts who cover us issues an adverse opinion about our company, our stock price would likely decline. If one or more of these analysts ceases research coverage of us or fails to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

***Future sales of our common stock in the public market could cause our stock price to fall.***

Our stock price could decline as a result of sales of a large number of shares of our common stock after this offering or the perception that these sales could occur. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

Upon completion of this offering and the concurrent private placements, 35,096,265 shares of our common stock will be outstanding (or 35,996,265 shares of common stock will be outstanding assuming exercise in full of the underwriters' option to purchase additional shares), based on our shares outstanding as of March 31, 2016. All shares of common stock expected to be sold in this offering will be freely tradable without restriction or further registration under the Securities Act of 1933, as amended, or Securities Act, unless held by our "affiliates," as that term is defined in Rule 144 under the Securities Act. The resale of the remaining 29,096,265 shares, or 82.9% of our outstanding shares after this offering, is currently prohibited or otherwise restricted as a result of securities law provisions, market standoff agreements entered into by our stockholders with us or lock-up agreements entered into by our stockholders with the underwriters. However, subject to applicable securities law restrictions and excluding shares of restricted stock that will remain unvested, these shares will be able to be sold in the public market beginning 180 days after the date of this prospectus. Shares of unvested restricted stock that were issued and outstanding as of the date of this prospectus will become available for sale immediately upon the vesting of such shares, as applicable, and the expiration of any applicable market stand-off or lock-up agreements. Shares issued upon the exercise of stock options pursuant to future awards that may be granted under our equity incentive plans or pursuant to future awards granted under those plans will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market stand-off and lock-up agreements, and Rule 144 and Rule 701 under the Securities Act. For more information see the section entitled "Shares Eligible for Future Sale" appearing elsewhere in this prospectus.

Upon completion of this offering and the concurrent private placements, the holders of approximately 25,051,650 shares, or 71.4%, of our common stock, will have rights, subject to some conditions, to require us to file registration statements covering the sale of their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register the offer and sale of all shares of common stock that we may issue under our equity compensation plans. Once we register the offer and sale of shares for the holders of registration rights and shares to be issued under our equity incentive plans, they can be freely sold in the public market upon issuance, subject to the lock-up agreements described in the section entitled "Underwriting" appearing elsewhere in this prospectus.

In addition, in the future, we may issue additional shares of common stock or other equity or debt securities convertible into common stock in connection with a financing, acquisition, litigation settlement, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

***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.***

Our executive officers, directors and principal stockholders, together with their respective affiliates, beneficially owned approximately 83.2% of our capital stock as of March 31, 2016. Upon completion of this offering and the concurrent private placements, that group will beneficially own 70.4% of our capital stock, of which 8.4% will be beneficially owned by our executive officers (assuming no exercise of the underwriters' option to purchase additional shares and excluding that group's participation in this offering). Accordingly, after this offering, our executive officers, directors and principal stockholders, if they choose to act together, will be able to determine the composition of the board of directors, retain the voting power to approve all matters requiring stockholder approval, including mergers and other business combinations, and continue to have significant influence over our operations. This concentration of ownership could have the effect of delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us that you may believe are in your best interests as one of our stockholders. This in turn could have a material adverse effect on our stock price and may prevent attempts by our stockholders to replace or remove the board of directors or management.

***If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.***

The initial public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent shares subsequently are issued under outstanding options or warrants, you will incur further dilution. Based on the initial public offering price of $18.00 per share and the sale of shares of common stock in the concurrent private placements, you will experience immediate dilution of $11.73 per share, representing the difference between our pro forma as adjusted net tangible book value per share, which gives effect to this offering and the concurrent private placements, and the initial public offering price. In addition, purchasers of common stock in this offering will have contributed approximately 43.6% of the aggregate price paid by all purchasers of our stock but will own only approximately 17.1% of our common stock outstanding after this offering.

***Our management team has broad discretion to use the net proceeds from this offering and its investment of these proceeds may not yield a favorable return. They may invest the proceeds of this offering in ways with which investors disagree.***

We expect to use the net proceeds from this offering to advance the research and development of our sentinel indications, to progress additional therapeutic candidates and for working capital and other general corporate purposes. We may also use a portion of the net proceeds to acquire, license and invest in complementary products, technologies or businesses; however, we currently have no agreements or commitments to complete any such transaction. However, within the scope of our plan, and in light of the various risks to our business that are set forth in this section, our management will have broad discretion over the use of proceeds from this offering, and we could spend the proceeds from this offering in ways our stockholders may not agree with or that do not yield a favorable return, if at all. If we do not invest or apply the proceeds of this offering in ways that improve our operating results, we may fail to achieve expected financial results, which could cause our stock price to decline.

***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 bylaws to be effective upon consummation of this offering 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 bylaws will:

- 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 will provide 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 will provide 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 bylaws, 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 will incur increased costs as a result of operating as a public company.***

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company, including costs associated with public company reporting requirements. We also anticipate that we will incur costs associated with relatively recently adopted corporate governance requirements, including requirements of the Securities and Exchange Commission, or SEC, and the NASDAQ Global Market. We expect these rules and regulations to increase our legal and financial compliance costs and to make some activities more time-consuming and costly. We also expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors or as executive officers. We are currently evaluating and monitoring developments with respect to these rules, and we cannot predict or estimate the amount of additional costs we may incur or the timing of such costs.

We are an emerging growth company, and, for as long as we continue to be an emerging growth company, we may choose to take advantage of exemptions from various reporting requirements applicable to other public companies but not to "emerging growth companies." We could remain an "emerging growth company" for up to five years, or until the earliest of (1) the last day of the first fiscal year in which our annual gross revenue exceeds $1 billion, (2) the date that we become a "large accelerated filer" as defined in Rule 12b-2 under the Securities Exchange Act of 1934, which would occur if the market value of our common stock that is held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter or (3) the date on which we have issued more than $1 billion in non-convertible debt during the preceding three-year period. So long as we remain an "emerging growth company," we expect to avail ourselves of the exemption from the requirement that our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting under Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404. When our independent registered public accounting firm is required to undertake an assessment of our internal control over financial reporting, the cost of our compliance with Section 404 will correspondingly increase. Moreover, if we are not able to comply with the requirements of Section 404 applicable to us in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the sections entitled "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business," contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus include, but are not limited to, statements about:

- 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 a pipeline of product candidates;
- our ability to advance any product candidates into, and successfully complete, clinical studies;
- our ability to advance our therapeutic delivery capabilities;
- the issuance of regulatory guidance regarding preclinical and clinical studies for gene 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;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our 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 or obtain additional grant 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."

In some cases, forward-looking statements can be identified by terminology such as "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section entitled "Risk Factors" and elsewhere in this prospectus. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this prospectus and the documents that we

reference in this prospectus and have filed with the Securities and Exchange Commission as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

This prospectus includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. We are responsible for all of the disclosure contained in this prospectus, and we believe these industry publications and third-party research, surveys and studies are reliable.

## USE OF PROCEEDS

We estimate that our net proceeds from the sale of shares of our common stock in this offering will be approximately $97.8 million, or $112.9 million if the underwriters exercise in full their option to purchase additional shares, based on the initial public offering price of $18.00 per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We currently intend to use the net proceeds from this offering as follows:

- $25.0 million to advance the research and development of our product candidates for our sentinel indications through to the submission of at least one IND;
- $15.0 million to progress additional *in vivo* and *ex vivo* pipeline product candidates;
- $10.0 million to further develop our delivery technologies and CRISPR/Cas9 gene editing platform; and
- the remainder for working capital and other general corporate purposes.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. For example, we may use a portion of the net proceeds for the acquisition of businesses or technologies to continue to build our therapeutic delivery, research and development capabilities and our intellectual property position, although we currently have no agreements, commitments or understandings with respect to any such transaction. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering and the concurrent private placements or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our research and development, the status of and results from non-clinical studies or clinical trials we may commence in the future, as well as any collaborations that we may enter into with third parties for our product candidates or strategic opportunities that become available to us, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering and the concurrent private placements.

Pending our use of proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation instruments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

## DIVIDEND POLICY

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

## REORGANIZATION

On August 20, 2015, we completed a series of transactions pursuant to which Intellia Therapeutics, LLC, our former sole stockholder and holding company parent, merged with and into us, and we continued to exist as the surviving corporation. Throughout this prospectus, we refer to these transactions and the related transactions enumerated below collectively as the "Reorganization." To consummate the Reorganization, we filed a certificate of merger with the Secretary of State of the State of Delaware. In connection with the Reorganization:

- holders of Intellia Therapeutics, LLC's outstanding Class A-2 preferred units received one share of our Series A-2 preferred stock for each Class A-2 preferred unit held immediately prior to the Reorganization, with an aggregate of 3,999,999 shares of our Series A-2 preferred stock issued in the Reorganization;
- holders of Intellia Therapeutics, LLC's outstanding Class A-1 preferred units received one share of our Series A-1 preferred stock for each Class A-1 preferred unit held immediately prior to the Reorganization, with an aggregate of 8,571,429 shares of our Series A-1 preferred stock issued in the Reorganization;
- holders of Intellia Therapeutics, LLC's outstanding Junior preferred units received one share of our Junior preferred stock for each Junior Preferred Unit held immediately prior to the Reorganization, with an aggregate of 8,110,599 shares of our Junior preferred stock issued in the Reorganization;
- holders of Intellia Therapeutics, LLC's outstanding common units received one share of our founder stock for each common unit held immediately prior to the Reorganization, with an aggregate of 2,298,000 shares of our founder stock issued in the Reorganization; and
- holders of Intellia Therapeutics, LLC's outstanding incentive units received shares of our restricted common stock in an amount equal in value to the value of such incentive units as determined by the applicable provisions of the Intellia Therapeutics, LLC operating agreement in effect immediately prior to the Reorganization, with an aggregate of 2,558,755 shares of our restricted common stock issued in the Reorganization.

Our Series A-2 preferred stock, Series A-1 preferred stock, Junior preferred stock and founder stock are designated as preferred stock under our amended and restated certificate of incorporation. All outstanding shares of our preferred stock convert to shares of common stock on a one-for-0.6465903 basis.

In connection with the Reorganization, by operation of law, we acquired all assets of Intellia Therapeutics, LLC and assumed all of its liabilities and obligations. The purpose of the Reorganization was to reorganize our corporate structure so that our company would continue as a corporation and so that our existing investors would own our capital stock rather than equity interests in a limited liability company. For the convenience of the reader, except as context otherwise requires, all information included in this prospectus is presented giving effect to the Reorganization.

## CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of December 31, 2015:

- on an actual basis;
- on a pro forma basis to give effect to (i) the conversion of all outstanding shares of our preferred stock into an aggregate of 23,481,956 shares of common stock immediately prior to the completion of this offering and (ii) the filing and effectiveness of our amended and restated certificate of incorporation upon the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to (i) our sale in this offering of 6,000,000 shares of common stock at the initial public offering price of $18.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, and (ii) our sale of 3,055,554 shares of common stock in the concurrent private placements to Regeneron and Novartis.

The following table should be read together with "Management's Discussion and Analysis of Financial Condition and Results of Operations," "Description of Capital Stock," and the consolidated financial statements and related notes appearing elsewhere in this prospectus.

| | As of December 31, 2015 | | |
|---|---|---|---|
| | Actual | Pro Forma | Pro Forma As Adjusted(1) |
| | (in thousands, except share and per share data) | | |
| Cash and cash equivalents | $ 75,816 | $ 75,816 | $ 228,656 |
| Convertible preferred stock (Series B, Series A-2, Series A-1, Junior and Founder), $0.0001 par value; 36,500,000 shares authorized, 36,316,628 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted | $ 88,557 | $ — | $ — |
| Stockholders' (deficit) equity: | | | |
| Preferred stock, $0.0001 par value; no shares authorized, issued or outstanding, actual; 5,000,000 shares authorized, no shares issued or outstanding, pro forma and pro forma as adjusted | — | — | — |
| Common stock, $0.0001 par value; 50,000,000 shares authorized, 2,558,755 shares issued and outstanding, actual; 120,000,000 shares authorized, 26,040,711 shares issued and outstanding, pro forma; 120,000,000 shares authorized, 35,096,265 shares issued and outstanding, pro forma as adjusted | — | 3 | 4 |
| Additional paid-in capital | 735 | 89,289 | 242,128 |
| Accumulated deficit | (21,936) | (21,936) | (21,936) |
| Total stockholders' (deficit) equity | (21,201) | 67,356 | 220,196 |
| Total capitalization | $ 67,356 | $ 67,356 | $ 220,196 |

(1) Pro forma as adjusted amounts do not include a $75.0 million upfront payment received from Regeneron in April 2016 under our license and collaboration agreement.

The actual, pro forma and pro forma as adjusted information set forth in the table excludes:

- 496,539 shares of common stock reserved for future issuance as of March 31, 2016 under our 2015 Plan, which was amended and restated as our 2015 Restated Plan, in connection with the effectiveness of the registration statement of which this prospectus is a part;

- 2,617,932 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2016, at a weighted average exercise price of $6.69 per share; and
- an additional 2,001,579 shares of common stock that will be made available for future issuance under our equity compensation plans upon the closing of this offering.

## DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value as of December 31, 2015 was $67.4 million, or $26.32 per share of our common stock. Our historical net tangible book value is the amount of our total tangible assets less our total liabilities. Historical net tangible book value per share represents historical net tangible book value divided by the 2,558,755 shares of our common stock outstanding as of December 31, 2015.

Our pro forma net tangible book value as of December 31, 2015 was $67.4 million, or $2.59 per share of our common stock. Pro forma net tangible book value per share represents historical net tangible book value divided by the total number of shares of common stock outstanding as of December 31, 2015, after giving effect to the conversion of all shares of our preferred stock then outstanding into 23,481,956 shares of common stock upon the closing of this offering.

After giving further effect to the sale of 6,000,000 shares of common stock that we are offering at the initial public offering price of $18.00 per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us and the sale of 3,055,554 shares of common stock in the concurrent private placements to Regeneron and Novartis at the initial public offering price of $18.00 per share, our pro forma as adjusted net tangible book value as of December 31, 2015 would have been approximately $220.2 million, or approximately $6.27 per share. This amount represents an immediate increase in pro forma net tangible book value of $3.68 per share to our existing stockholders and an immediate dilution in pro forma net tangible book value of approximately $11.73 per share to investors participating in this offering.

Dilution per share to investors participating in this offering is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the initial public offering price per share paid by investors participating in this offering. The following table illustrates this dilution (without giving effect to any exercise by the underwriters of their over-allotment option):

| | | |
|---|---|---|
| Initial public offering price per share | | $18.00 |
| Historical net tangible book value per share as of December 31, 2015 | $ 26.32 | |
| Pro forma decrease in historical net tangible book value per share attributable to pro forma adjustments described in preceding paragraphs | (23.73) | |
| Pro forma net tangible book value per share as of December 31, 2015 | 2.59 | |
| Increase in pro forma net tangible book value per share attributable to investors participating in this offering | 2.57 | |
| Pro forma as adjusted net tangible book value per share after this offering | | 5.16 |
| Pro forma as adjusted net tangible book value per share after this offering and the concurrent private placements | | $ 6.27 |
| Dilution per share to investors participating in this offering | | $11.73 |

If the underwriters exercise their option to purchase additional shares of common stock in this offering in full at the initial public offering price of $18.00 per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, the pro forma as adjusted net tangible book value would be $6.54 per share, and the dilution in pro forma net tangible book value per share to investors in this offering would be $11.46 per share.

The following table summarizes, on a pro forma as adjusted basis, as of December 31, 2015, the difference between the number of shares of common stock purchased from us, the total consideration paid to us and the average price per share paid by existing stockholders and by investors in this offering and the concurrent private placements at the initial public offering price of $18.00 per share, before deducting underwriting discounts and commissions and estimated offering expenses payable by us.

| | Shares Purchased | | Total Consideration | | Average Price Per Share |
|---|---|---|---|---|---|
| | Number | Percent | Amount | Percent | |
| | (in thousands except per share data) | | | | |
| Existing stockholders(1) | 26,040,711 | 74% | $ 85,017,155 | 34% | $ 3.26 |
| Concurrent private placement investors | 3,055,554 | 9 | 54,999,972 | 22 | $ 18.00 |
| Investors in this offering | 6,000,000 | 17 | 108,000,000 | 44 | $ 18.00 |
| Total | 35,096,265 | 100.0% | $248,017,127 | 100.0% | |

(1) We expect that certain of our existing stockholders, including certain affiliates of our directors, will purchase an aggregate of $45.6 million of shares of our common stock in this offering at the initial public offering price. The presentation in this table regarding ownership by existing stockholders does not give effect to any purchases in this offering by such stockholders.

The above discussion and tables are based on shares of common stock issued and outstanding as of December 31, 2015 and (i) includes 23,481,956 additional shares of our common stock issuable upon the conversion of all outstanding shares of our preferred stock into shares of common stock upon the closing of this offering and (ii) excludes:

- 496,539 shares of common stock reserved for future issuance as of March 31, 2016 under our 2015 Plan, which was amended and restated as our 2015 Restated Plan, in connection with the effectiveness of the registration statement of which this prospectus is a part;
- 2,617,932 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2016, at a weighted average exercise price of $6.69 per share; and
- an additional 2,001,579 shares of common stock that will be made available for future issuance under our equity compensation plans upon the closing of this offering.

To the extent that outstanding options are exercised or shares are issued under our 2015 Restated Plan, you will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities may result in further dilution to our stockholders.

## SELECTED CONSOLIDATED FINANCIAL DATA

*The following selected historical consolidated financial data should be read together with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the consolidated financial statements, related notes and other financial information included elsewhere in this prospectus. The selected consolidated financial data in this section are not intended to replace the consolidated financial statements and are qualified in their entirety by the consolidated financial statements and related notes included elsewhere in this prospectus.*

We have derived the selected consolidated statement of operations data for the period from May 7, 2014 (inception) to December 31, 2014 and the year ended December 31, 2015 and the selected consolidated balance sheet data as of December 31, 2014 and 2015 from our audited consolidated financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of results that may be expected in the future.

| | Period from May 7, 2014 (inception) to December 31, 2014 | Year Ended December 31, 2015 |
|---|---|---|
| | (in thousands, except per unit and per share data) | |
| **Consolidated Statements of Operations Data:** | | |
| Collaboration revenue | $ — | $ 6,044 |
| Operating expenses: | | |
| Research and development | 1,105 | 11,170 |
| In-process research and development | 6,055 | — |
| General and administrative | 2,379 | 8,283 |
| Total operating expenses | 9,539 | 19,453 |
| Loss before income taxes | (9,539) | (13,409) |
| Benefit from income taxes | — | 1,012 |
| Net loss | $ (9,539) | $ (12,397) |
| Net loss per common unit, basic and diluted | $ (11.55) | $ — |
| Net loss per share attributable to common stockholders, basic and diluted | $ — | $ (51.02) |
| Weighted average common units outstanding, basic and diluted | 826 | — |
| Weighted average shares outstanding, basic and diluted | — | 243 |
| Pro forma net loss per share, basic and diluted (unaudited)(1) | | $ (0.70) |
| Pro forma weighted average shares outstanding, basic and diluted (unaudited)(1) | | 17,664 |

| | As of December 31, 2014 | As of December 31, 2015 |
|---|---|---|
| | (in thousands) | |
| **Consolidated Balance Sheet Data:** | | |
| Cash and cash equivalents | $ 9,845 | $ 75,816 |
| Working capital(2) | 7,775 | 66,931 |
| Total assets | 10,694 | 82,139 |
| Deferred revenue | — | 10,312 |
| Convertible preferred stock | — | 88,557 |
| Total stockholders' equity (deficit) | 7,566 | (21,201) |

(1) Basic and diluted pro forma net loss per share give effect to the conversion of all shares of preferred stock issued in connection with the Reorganization into shares of common stock immediately prior to the completion of this offering, assuming such conversion occurred on the later of May 7, 2014 (inception) or the issuance date of the corresponding unit that converted to preferred stock in the Reorganization.

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

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*The following discussion and analysis of our financial condition and results of operations should be read together with our consolidated financial statements and related notes and other financial information appearing elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this prospectus, 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.*

*As more fully described in the section entitled "Reorganization" appearing elsewhere in this prospectus, on August 20, 2015, we completed transactions pursuant to which Intellia Therapeutics, LLC merged with and into Intellia Therapeutics, Inc., with Intellia Therapeutics, Inc. continuing as the surviving corporation. In connection with the Reorganization, all of the outstanding common and preferred unitholders of Intellia Therapeutics, LLC became holders of preferred stock of Intellia Therapeutics, Inc., and holders of incentive units in Intellia Therapeutics, LLC received restricted common stock in Intellia Therapeutics, Inc.*

### Overview

We are a leading gene editing company focused on the development of proprietary, potentially curative therapeutics utilizing a recently developed 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 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 gene editing and develop a potential new class of therapeutic products.

We believe our strong 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 gene editing-based therapeutics. To maximize our opportunity to rapidly develop clinically successful products, we have applied a risk-mitigated approach to selecting our initial indications, which we refer to as our sentinel indications. Our approach is defined by four primary axes: (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 sentinel indications include *in vivo* programs focused on diseases of the liver that have significant unmet medical needs – transthyretin amyloidosis, which we are co-developing with Regeneron Pharmaceuticals, Inc., or Regeneron, alpha-1 antitrypsin deficiency, hepatitis B virus and inborn errors of metabolism – as well as *ex vivo* applications of the technology in chimeric antigen receptor T cell, or CAR T cell, and hematopoietic stem cell, or HSC, product candidates which are selectively partnered with our collaborator, Novartis Institutes for BioMedical Research Inc., or Novartis.

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 studies and evaluating a clinical path for our pipeline programs. To date, we have financed our operations primarily through private placements of our equity securities and funding received from our collaboration and license agreement with Novartis. All of our revenue to date has been collaboration revenue. Since our inception and through December 31, 2015, we have raised an aggregate of approximately $104.0 million to fund our operations, of which approximately $19.0 million was through our collaboration with Novartis and approximately $85.0 million was from the sale of our equity, principally preferred securities. In addition, we received $75.0 million in the form of an upfront payment under our collaboration with Regeneron in April 2016.

Since inception, we have incurred operating losses. Our net loss was $9.5 million for the period from May 7, 2014 (inception) to December 31, 2014, primarily as a result of the cost of obtaining in-licensed CRISPR/Cas9 intellectual property, and $12.4 million for the year ended December 31, 2015. As of December 31, 2015, we had

an accumulated deficit of $21.9 million. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we: advance the programs for our sentinel indications toward clinical development; continue the research and development of our other potential product candidates and delivery modalities; seek to discover and develop additional product candidates; seek regulatory approvals for any product candidates that successfully complete clinical trials; ultimately establish a sales, marketing and distribution infrastructure and scale up external and/or internal manufacturing capabilities to commercialize any products for which we may obtain regulatory approval; maintain, expand and protect our intellectual property portfolio; hire additional clinical, regulatory and scientific personnel; and add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

**Collaborations**

In December 2014, we entered into a strategic collaboration and license agreement with Novartis focused on the development of new *ex vivo* CRISPR/Cas9-based therapies using CAR T cells and HSCs. Under the terms of our agreement, we received a $10.0 million upfront technology access payment in January 2015. In addition, we are entitled to receive $20.0 million in additional technology access fees and up to $20.0 million in research payments, in the aggregate, over the five-year collaboration term. For each product under the collaboration, 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 U.S. and the European Union, or 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 retain exclusive rights to research a limited number of HSC targets for our proprietary pipeline. In addition, prior to our entry into our collaboration with Novartis, we entered into an exclusivity agreement with Novartis pursuant to which we agreed to issue preferred securities to Novartis. We received $9.0 million from the sale of such securities to Novartis. We also received approximately $4.0 million from the sale of Series B preferred stock to Novartis in our Series B preferred stock financing. See the section entitled "Certain Relationships and Related Party Transactions" appearing elsewhere in this prospectus for more information.

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 the terms of our agreement 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 the low teens, in each case, on a per-product basis, which royalties are potentially subject to various reductions and offsets and are further subject to our existing low single-digit royalty obligations under our Caribou license 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 agreement with Novartis. In December 2014, we entered into a five-year strategic collaboration and license agreement with Novartis focused on the development of *ex vivo* CRISPR/Cas9-based therapies using CAR T cells and HSCs. Under the terms of the agreement, we received a $10.0 million upfront technology access payment and $9.0 million from the sale of preferred securities to Novartis, which were

determined to have a fair value of $11.6 million. In addition, we are entitled to receive an additional $20.0 million in technology access fees and up to $20.0 million in research payments.

Going forward, our revenue will also include collaboration revenue, including amounts recognized related to upfront payments, earned under our collaboration and license agreement with Regeneron. In April 2016, we entered into a strategic collaboration and license agreement with Regeneron focused on the development of *in vivo* CRISPR/Cas-based therapeutic products primarily directed to gene editing in the liver as well as technology advances to the CRISPR/Cas platform. Under the terms of the agreement, we received a nonrefundable $75.0 million upfront payment.

In addition, we are also eligible to receive additional milestone payments and royalties under both collaboration agreements as further described in the section entitled "Business – Collaborations" appearing elsewhere in this prospectus.

***Research and Development***

Research and development expenses consist of expenses incurred in performing research and development activities, including the cost to obtain licenses to intellectual property, compensation and benefits, including equity-based compensation, for full-time research and development employees, facility-related expenses, overhead expenses, lab supplies and contract research services, including research services provided to us by Caribou Biosciences, Inc., or Caribou, pursuant to a services agreement, or the Caribou services agreement, we entered into with Caribou in July 2014. See the section entitled "Certain Relationships and Related Party Transactions – License Agreement and Services Agreement with Caribou Biosciences, Inc." appearing elsewhere in this prospectus for more information. In the early phases of development, our research and development costs are often devoted to product platform and proof-of-concept studies that are not necessarily allocable to a specific target; therefore, we have not yet begun tracking our expenses on a program-by-program basis.

***In-Process Research and Development***

In-process research and development expense represents the cost of acquiring in-process research and development rights to our fundamental CRISPR/Cas9 intellectual property from Caribou.

***General and Administrative***

General and administrative expenses consist primarily of salaries and benefits, including equity-based compensation, for our executive, finance, intellectual property, 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.

**Results of Operations for the Period from May 7, 2014 (Inception) to December 31, 2014 and the Year Ended December 31, 2015**

***Collaboration Revenue***

In December 2014, we entered into a five-year strategic collaboration and license agreement with Novartis focused on the development of *ex vivo* CRISPR/Cas9-based therapies using CAR T cells and HSCs. Under the terms of the agreement, we received a $10.0 million upfront technology access payment and $9.0 million from the sale of preferred securities to Novartis, which were determined to have a fair value of $11.6 million. In addition, we are entitled to receive an additional $20.0 million in technology access fees and up to $20.0 million in research payments. We are also eligible to receive additional milestone payments, option fees and royalties as further described in the section entitled "Business – Collaborations."

We determined the fixed portion of consideration under the arrangement to be the $30.0 million of total technology access fees, for which there are no contingent terms. Of the $30.0 million in fixed consideration, $2.6 million was allocated to the preferred securities issued to Novartis, representing the difference between the

price paid for these securities and their fair values at date of issuance. We are recognizing the net consideration of $27.4 million as collaboration revenue over the five-year performance period of the arrangement. We recognized collaboration revenue of $6.0 million in the year ended December 31, 2015, representing the recognition of these amounts from deferred revenue. We did not recognize any collaboration revenue in 2014.

***Research and Development***

We recorded $11.2 million in research and development expenses during the year ended December 31, 2015, compared to $1.1 million in the period from May 7, 2014 (inception) to December 31, 2014. Research and development expenses in the period from May 7, 2014 (inception) to December 31, 2014 consisted primarily of third-party research services under the Caribou services agreement and personnel-related costs for our internal research and development staff and related expenses, including salaries, benefits and equity-based compensation. The $11.2 million in research and development expenses during the year ended December 31, 2015 was primarily comprised of salaries and related costs for our research and development team, which grew from three employees as of December 31, 2014 to 38 employees as of December 31, 2015, third-party research service fees under the Caribou service agreement and laboratory supplies and materials for internal use. We expect research and development expenses to increase as we continue to grow our research and development team and continue to advance our research plans.

***In-Process Research and Development***

Our $6.1 million in in-process research and development expenses for the period from May 7, 2014 (inception) to December 31, 2014 represented the cost of acquiring in-process research and development rights to our foundational CRISPR/Cas9 intellectual property from Caribou. We did not record any in-process research and development expense in the year ended December 31, 2015.

***General and Administrative***

We recorded $8.3 million in general and administrative expenses during the year ended December 31, 2015, compared to $2.4 million in the period from May 7, 2014 (inception) to December 31, 2014. Our $2.4 million in general and administrative expenses for the period from May 7, 2014 (inception) to December 31, 2014 primarily related to our internal general and administrative salaries and related expenses, legal, patent and consulting fees associated with our initial start-up and costs incurred to pay 30.0% of Caribou's patent prosecution filing and maintenance costs for our licensed intellectual property pursuant to the license agreement with Caribou. The $8.3 million in general and administrative expenses during the year ended December 31, 2015 was primarily comprised of salaries and benefits costs as well as audit, consulting and professional fees, including legal fees and intellectual property costs, such as amounts incurred resulting from our obligation to pay 30.0% of Caribou's patent prosecution filing and maintenance costs for our licensed intellectual property. We expect general and administrative expenses to continue to increase as we grow our organization, including, upon any successful completion of this offering, as we incur additional costs associated with being a publicly traded company, including increased legal, accounting and corporate governance costs.

***Benefit from Income Taxes***

We did not recognize any benefit from income taxes during the period from May 7, 2014 (inception) to December 31, 2014. 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 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, 2015, we have raised an aggregate of $104.0 million to fund our operations, of which $19.0 million was through our collaboration with Novartis and $85.0 million was from the sale of equity securities. As of December 31, 2015, we had $75.8 million in cash and cash equivalents.

We are entitled to receive technology access fees and research payments under our collaboration with Novartis and received a $75.0 million upfront payment under our collaboration with Regeneron. We are also eligible to earn a significant amount of milestone payments and royalties, in each case, on a per-product basis under our collaborations with Novartis and 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 agreement 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. 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 and as we begin to occupy our new office and laboratory facility. In addition, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company.

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 cash needs through a combination of equity or debt 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 collaborations with Novartis and Regeneron. Except for these sources of funding, upon completion of this offering, we will not have any committed external source of liquidity. To the extent that we raise additional capital through the future sale of equity or debt securities, 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 or debt 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 timing expectations related to the progress of our programs, we expect that the net proceeds from this offering, the upfront payment and concurrent private placement with Regeneron and the concurrent private placement with Novartis, together with our existing cash and cash equivalents as of December 31, 2015 as well as technology access and research funding that we expect to receive from Novartis, will enable us to fund our operating expenses and capital expenditures for at least the next 36 months, without giving effect to any potential milestone payments or extension fees we may receive under our collaboration agreements with Novartis and Regeneron. We have based this estimate on 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 table summarizes our cash flows for the period from May 7, 2014 (inception) to December 31, 2014 and the year ended December 31, 2015:

| | Period from May 7, 2014 (inception) to December 31, 2014 | Year Ended December 31, 2015 |
|---|---|---|
| | (in thousands) | |
| Net cash used in operating activities | $ (2,322) | $ (1,763) |
| Net cash used in investing activities | (575) | (2,554) |
| Net cash provided by financing activities | 12,742 | 70,288 |

***Net Cash Used in Operating Activities***

Net cash used in operating activities of $2.3 million during the period from May 7, 2014 (inception) to December 31, 2014 consisted primarily of compensation and related expenses as well as legal and consulting costs incurred with the initial phases of establishing our company's operations and early research activities performed by Caribou. Net cash used in operating activities of $1.8 million in the year ended December 31, 2015 primarily reflected compensation, lab and professional service expenses as well as amounts paid by us under the Caribou services agreement during the period, partially offset 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 Cash Used in Investing Activities***

Net cash used in investing activities during the periods from May 7, 2014 (inception) to December 31, 2014 related primarily to the July 2014 acquisition of in-process research and development rights to our foundational CRISPR/Cas9 intellectual property from Caribou, as well as the purchase of property and equipment in connection with our move to our office space in Cambridge, Massachusetts. Purchases of property and equipment increased during the year ended December 31, 2015 as we completed the build-out of this office and laboratory space. We expect purchases of property and equipment to increase in 2016 as we begin the build-out of our new office and laboratory facility.

***Net Cash Provided by Financing Activities***

Net cash provided by financing activities related to the sale of preferred securities in all periods presented. In June 2014, we sold shares of common stock to Atlas Venture Fund IX, LP, or Atlas Venture Fund IX, for net proceeds of $0.1 million. In the remainder of 2014, we issued common and preferred securities to Atlas Venture Fund IX and Novartis for aggregate net proceeds of $12.6 million. In the year ended December 31, 2015, we completed the sale of preferred securities to Atlas Venture Fund IX, for net proceeds of $2.0 million, received $2.6 million in consideration from Novartis related to their purchase of preferred securities from us and completed the sale of preferred securities to new and existing investors for aggregate net proceeds of $67.4 million.

**Contractual Obligations and Contingent Liabilities**

The following summarizes our contractual obligations as of December 31, 2015:

| | Payments Due by Period | | | | |
|---|---|---|---|---|---|
| | Total | Less than 1 Year | 1 to 3 Years | 3 to 5 Years | More than 5 Years |
| | (in thousands) | | | | |
| Fixed payments to Caribou | $1,500 | $1,500 | $ — | $ — | $ — |
| Property leases | 3,755 | 945 | 1,868 | 942 | — |
| Total contractual obligations | $5,255 | $2,445 | $1,868 | $942 | $ — |

- *Fixed payments to Caribou.* Represents obligations by us to make fixed payments under the Caribou services agreement.
- *Property leases.* Represents future minimum lease payments under non-cancelable operating leases in effect as of December 31, 2015. 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 specified human therapeutic applications, due to the uncertainty of the occurrence of the events requiring payment under that agreement. The table also excludes (i) the property lease we entered into subsequent to December 31, 2015 and (ii) 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.

In January 2016, we 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. Our contractual commitments under the committed first six years of this lease total $28.3 million. Payments under the contract are expected to begin in late 2016 when we are projected to gain access to the space.

Under the Caribou license agreement, we sublicense a patent family that is currently subject to interference proceedings declared by the Patent Trial and Appeal Board of the United States Patent and Trademark Office. If our sublicensed patent family does not prevail in these proceedings, claims could be asserted against us during development or commercialization of a product that relies on this technology. 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.

**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 United States of America. 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 United States of America 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 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 performed 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 complete 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 agreement, 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 collaboration. Our primary performance obligations under this collaboration 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 and recognize equity-based compensation expense, net of estimated forfeitures, on a straight-line basis over the requisite service period of the awards, which is generally the vesting period of the respective award. Compensation expense is recognized for only the portion of awards that are expected to vest. In developing a forfeiture rate estimate, we have considered our historical experience to estimate pre-vesting forfeitures for service-based awards. We estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from those estimates.

We measure equity awards granted to consultants and non-employees based on the fair value of the award on the date of grant. 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 the common or incentive securities.

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.

*Determination of the Fair Value of Equity Securities*

As there has been no public market for our common or incentive units and common stock to date, the estimated fair value of our common and incentive units and common stock has been determined by our board of directors as of the date of each award grant, with input from management, considering our most recently available third-party valuations of common and incentive units and common stock and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Our common and incentive security valuations were prepared using either an option-pricing method, or OPM, or a probability-weighted expected return method, or PWERM, which used a combination of market approaches and an income approach to estimate our enterprise value. The OPM treats common securities and preferred securities as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common and incentive units and common stock have value only if the funds available for distribution to members exceeded the value of the preferred security liquidation preference at the time of the liquidity event, such as a strategic sale or a merger. The PWERM is a scenario-based methodology that estimates the fair value of common and incentive units and common stock based upon an analysis of future values for the company, assuming various outcomes. The common and incentive units and common stock values are based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of common, incentive and preferred securities. The future

value of the common and incentive units and common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common and incentive units and common stock. These third-party valuations were performed at various dates, which resulted in valuations of our common and incentive units of $0.63 and $0.22 per share, respectively, as of July 31, 2014 and $1.97 and $1.34 per share, respectively, as of December 31, 2014 and valuations of our common stock of $5.81, $6.40 and $6.83 per share as of July 20, 2015, November 30, 2015 and January 29, 2016, respectively. In addition to considering the results of these third-party valuations, our board of directors considered various objective and subjective factors to determine the fair value of our common and incentive units and common stock as of each grant date, which may be a date later than the most recent third-party valuation date, including:

- the prices of our preferred securities sold to or exchanged between outside investors in arm's length transactions, and the rights, preferences and privileges of our preferred securities as compared to those of our common and incentive units and common stock, including the liquidation preferences of our preferred securities;
- the progress of our research and development efforts, including the status of preclinical studies and planned clinical trials for our product candidates;
- the lack of liquidity of our equity as a private company;
- our stage of development and business strategy and the material risks related to our business and industry;
- the achievement of enterprise milestones, including entering into collaboration and license agreements;
- the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;
- any external market conditions affecting the biotechnology industry, and trends within the biotechnology industry;
- the likelihood of achieving a liquidity event for the holders of our common and incentive units and common stock, such as an initial public offering, or IPO, or a sale of our company, given prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our equity-based compensation expense could be materially different.

Following the closing of this offering, the fair value of our common stock will be determined based on the quoted market price of our common stock.

*Equity-Based Security Awards Granted*

The following table sets forth by grant date and type of award the number of securities granted since inception, which were granted for no returned consideration:

| Grant Date | Type of Award Granted | Number of Securities Underlying Grants | Grant Date Fair Value Per Unit or Share |
|---|---|---|---|
| July 31, 2014 | Common units | 1,351,763 | $ 0.63 |
| July 31, 2014 | Incentive units | 1,351,761 | $ 0.22 |
| October 1, 2014 | Incentive units | 159,031 | $ 1.34 |
| October 30, 2014 | Incentive units | 15,902 | $ 1.34 |
| November 12, 2014 | Incentive units | 15,902 | $ 1.34 |
| November 13, 2014 | Incentive units | 15,902 | $ 1.34 |
| April 15, 2015 | Incentive units | 546,760 | $ 1.34 |
| June 23, 2015 | Incentive units | 130,405 | $ 1.34 |
| June 29, 2015 | Incentive units | 83,822 | $ 1.34 |
| July 6, 2015 | Incentive units | 37,058 | $ 1.34 |
| July 13, 2015 | Incentive units | 79,411 | $ 1.34 |
| September 22, 2015 | Stock options | 270,558 | $ 5.81 |
| September 28, 2015 | Stock options | 1,588 | $ 5.81 |
| October 5, 2015 | Stock options | 8,823 | $ 5.81 |
| December 22, 2015 | Stock options | 175,405 | $ 6.40 |
| February 2, 2016 | Stock options | 80,828 | $ 6.83 |
| February 3, 2016 | Stock options | 2,080,730 | $ 6.83 |

***Emerging Growth Company Status***

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We are irrevocably choosing to "opt out" of this provision and, as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

***Recent Accounting Pronouncements***

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or 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 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. We expect that 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. In July 2015, the FASB voted to delay the effective date of this standard such that ASU 2014-09 will be effective for us for annual periods beginning after December 15, 2017 and for interim periods within those fiscal years. Early adoption of the standard is permitted for annual periods beginning after December 15, 2016. We are evaluating the impact that the adoption of ASU 2014-09 will have on our consolidated financial statements.

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern*. ASU 2014-15 amends Accounting Standards Codification, or ASC, 205-40, *Presentation of Financial Statements—Going Concern*, by providing guidance on determining when and how reporting entities must disclose going-concern uncertainties in their financial statements, including requiring management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date of issuance of the entity's financial statements and providing certain disclosures if there is

substantial doubt about the entity's ability to continue as a going concern. ASU 2014-15 will be effective for us for annual periods ending after December 15, 2016 and interim periods within annual periods beginning after December 15, 2016. We are evaluating the potential impact of this ASU on our consolidated financial statements but believe its adoption will have no impact on our financial position, results of operations or cash flows.

In February 2015, the FASB issued ASU No. 2015-02, *Consolidation (Topic 810)—Amendments to the Consolidation Analysis*. ASU 2015-02 modifies the existing consolidation guidance in ASC 810, *Consolidation*, by significantly changing the consolidation analysis reporting organizations are required to complete in determining whether to consolidate certain legal entities. ASU 2015-02 requires either a retrospective or modified retrospective approach to adoption and will be effective for us for annual periods beginning after December 15, 2015 and for interim periods within those fiscal years. We are evaluating the impact of the adoption of ASU 2015-02 on our consolidated financial statements but believe its adoption will have no material impact on our financial position, results of operations or cash flows.

In April 2015, the FASB issued ASU No. 2015-05, *Customer's Accounting for Fees Paid in a Cloud Computing Arrangement*. ASU 2015-05 amends ASC 350-40, *Internal-Use Software*, by providing customers with guidance on determining whether a cloud computing arrangement contains a software license that should be accounted for as internal-use software. ASU 2015-05 will be effective for us for annual periods beginning after December 15, 2015 and interim period within annual periods beginning after December 15, 2016. We are evaluating the impact that this ASU may have on our consolidated financial statements, if any.

In November 2015, the FASB issued ASU No. 2015-17, *Balance Sheet Classification of Deferred Taxes*. ASU 2015-17 amends ASC 740, *Income Taxes*, by requiring entities to present deferred tax assets and deferred tax liabilities as noncurrent in a classified balance sheet. ASU 2015-17 would be effective for annual periods beginning after December 15, 2016 and interim periods within those fiscal years. Early adoption is permitted. We elected to early adopt this guidance on a prospective basis beginning with our year ending as of December 31, 2015; however there was no material impact to our financial position as we carry a full valuation allowance.

In February 2016, the FASB issued ASU 2016-02, *Leases*. ASU 2016-02 amends ASC 840, *Leases*, by introducing a lessee model that requires balance sheet recognition of most leases. We are the lessee under certain leases that are accounted for as operating leases. The proposed changes would require that substantially all of our operating leases be recognized as assets and liabilities on our balance sheet. ASU 2016-02 will be effective for public companies for annual periods beginning after December 15, 2018 and interim periods within those fiscal years and for private companies for annual periods beginning after December 15, 2019 and interim periods within fiscal years beginning after December 15, 2020. We are evaluating the impact that the adoption of ASU 2016-02 will have on our consolidated financial statements.

**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.

**Quantitative and Qualitative Disclosures about Market Risk**

The market risk inherent in our financial instruments and in our financial position consists of the potential loss arising from adverse changes in interest rates. As of December 31, 2015, we had cash equivalents of $30.0 million consisting of interest-bearing money market accounts. 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 our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents.

We occasionally contract with vendors internationally. Transactions with these vendors are predominantly settled in U.S. dollars, and, therefore, we believe that we have only minimal exposure to foreign currency exchange risks. We do not hedge against foreign currency risks.

# BUSINESS

## Overview

We are a leading gene editing company focused on the development of proprietary, potentially curative therapeutics utilizing a recently developed biological tool known as the CRISPR/Cas9 system. We believe that the CRISPR/Cas9 technology has the potential to transform medicine by permanently editing disease-associated genes 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 gene 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 gene editing tool. Gene editing is the precise and targeted modification of the genetic material of cells. Since the publication of Dr. Doudna's landmark paper, more than 2,600 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 genes. 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. This approach has the potential to provide curative therapeutic options for patients with chronic diseases by addressing the underlying cause of the disease.

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* applications, in which cells are removed from a patient's body, modified using CRISPR/Cas9 and then returned to the patient. Initially, our *in vivo* pipeline includes proprietary programs targeting transthyretin amyloidosis, or ATTR, which we are co-developing with Regeneron Pharmaceuticals, Inc., or Regeneron, alpha-1 antitrypsin deficiency, or AATD, hepatitis B virus, or HBV, and inborn errors of metabolism, or IEMs. Our initial *ex vivo* pipeline includes both proprietary and partnered programs focused on chimeric antigen receptor T cells, or CAR T cells, and hematopoietic stem cells, or HSCs, the stem cells from which all of the various types of blood cells originate, which we are developing in collaboration with Novartis Institutes for BioMedical Research, Inc., or Novartis.

To maximize our opportunity to rapidly develop clinically successful products, we have applied a risk- mitigated approach to selecting our initial indications, which we refer to as our sentinel indications. Specifically, we have selected indications with significant unmet medical needs based on four primary axes:

- 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 modalities.

These selection criteria position us to build a risk-diversified pipeline, where 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 sentinel indications to inform our selection of subsequent indications and targets of interest. We believe this approach serves to increase our probabilities of success in our sentinel indications, generate insights that will accelerate the development of subsequent therapeutic products and broaden the opportunity for potential strategic alliances.

The following table illustrates our current discovery programs and opportunities:

| Programs | Partnerships | Type of Edit | Delivery | Upcoming Milestones |
|---|---|---|---|---|
| ***In Vivo*** | | | | |
| Transthyretin Amyloidosis (ATTR) | Co-developing with Regeneron | Knockout | LNP to Liver | Select 1 to 2 development candidates and advance to IND enabling studies in the next 12 to 24 months |
| Alpha-1 Antitrypsin Deficiency (AATD) | Proprietary | Knockout Repair | LNP to Liver | |
| Hepatitis B Virus (HBV) | Proprietary | Knockout | LNP to Liver | |
| Inborn Errors of Metabolism (IEMs) | Proprietary | Knockout Repair Insertion | LNP to Liver | |
| ***Ex Vivo*** | | | | |
| Hematopoietic Stem Cells (HSCs) | Selectively partnered with Novartis; proprietary | Knockout Repair Insertion | Electroporation | First Novartis IND expected to be submitted in 2018 |
| CAR T Cells | Partnered with Novartis | Knockout Insertion | Electroporation | Advance preclinical development |

Delivery plays a key role in our *in vivo* therapeutic approach. We have shown in animal models that lipid nanoparticle, or 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. With our team's expertise with LNP delivery technology, we expect to be able to readily translate the LNPs that we are using for our preclinical development to clinical development in humans. In parallel, we are exploring additional delivery vehicles, including viral delivery vectors, which are viruses engineered to carry non-viral nucleic acids to patients' cells, that we believe may assist us in targeting other organs.

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

- ATTR program, which utilizes a gene knockout strategy;
- AATD program, which utilizes either a gene knockout strategy or a gene repair strategy;
- HBV program, which utilizes a knockout strategy to target covalently closed circular DNA, or cccDNA; and
- IEM program, which has the potential to utilize all three editing approaches, including targeted DNA insertion.

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.

Our sentinel *ex vivo* programs in CAR T cell and HSC applications are being developed in partnership 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 modified *ex vivo* by inserting a chimeric antigen receptor, or 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 that has 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 pathways to positively modulate 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 express a therapeutic protein, which is then administered to patients in need of that protein. Our sentinel *ex vivo* programs will help inform the broader applicability of CRISPR/Cas9 in an *ex vivo* setting, which we plan to explore in eXtellia, a division of our company focused on the application of CRISPR/Cas9 gene editing in the fields of immuno-oncology beyond CAR T cells and autoimmune and inflammatory diseases. We expect eXtellia to focus on other relevant types of immune cells, such as natural killer, or NK, cells and tumor infiltrating lymphocytes, or TILs, for immuno-oncology applications, T regulatory cells, or Tregs, for autoimmune disorders and other cell types, including induced pluripotent stem cells, mesenchymal stem cells and muscle satellite stem cells for tissue-targeted treatments, for which we retain proprietary rights. Our *ex vivo* delivery approach is a clinically proven delivery method called electroporation, an electrical charge-based technique for delivering molecules into cells that is currently being 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 approach to selecting our sentinel *in vivo* and *ex vivo* programs positions us to build a pipeline across a range of indications and to generate a wealth of data that opens 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 gene editing technology 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.

To enable further development of our technology and *in vivo* and *ex vivo* programs, we completed a private placement for gross proceeds of $70.0 million of our Series B preferred stock in August 2015 led by OrbiMed Advisors LLC. Additional investors in this financing included Fidelity Management & Research, Janus Capital Management, Foresite Capital, Sectoral Asset Management Inc., EcoR1 Capital LLC, our existing investors, Atlas Venture Fund IX and Novartis, as well as other leading mutual fund and healthcare investors.

**Our Team**

We have assembled a world-class team of executives, founders and advisors who are dedicated to the development of CRISPR/Cas9-based therapeutic products for patients with significant unmet medical needs. Our team's expertise spans CRISPR/Cas9 and broader gene editing technologies, *in vivo* and *ex vivo* therapeutic delivery technologies, preclinical and clinical development, product scale-up and manufacturing, cell and molecular biology, intellectual property, finance and regulatory affairs.

Our executive team comprises leaders with proven track records of successfully translating scientific visions into tangible therapies, solving complex issues in delivering novel therapeutics and progressing new and novel therapies through regulatory approval. Our management team includes the following key individuals:

- ***Nessan Bermingham, Ph.D., our Founder, President and Chief Executive Officer***, who brings 15 years of experience in biotechnology investing and operational oversight across a number of companies, including UBS AG and most recently as a venture partner at Atlas Venture;
- ***Thomas M. Barnes, Ph.D., our Chief Scientific Officer***, who brings over 20 years of experience in drug discovery, including at Eleven Biotherapeutics Inc., Ore Pharmaceuticals, Inc. (formerly known as Gene Logic, Inc.) and Millennium Pharmaceuticals, Inc.;
- ***John M. Leonard, M.D., our Chief Medical Officer***, who, during 21 years at AbbVie Inc. and Abbott Laboratories, oversaw the development and approval of 15 medicines, including Humira and Kaletra;
- ***David V. Morrissey, Ph.D., our Chief Technology Officer***, who was instrumental in the development of LNP technology at Novartis and brings over 17 years of experience in drug development, including at Novartis, Sirna Therapeutics Inc., and Bristol-Myers Squibb;

- ***José E. Rivera, J.D., our Chief Operating Officer and Chief Legal Officer***, who brings 17 years of experience in managing complex legal issues in the biopharmaceutical and healthcare industries, including strategically developing, protecting and defending valuable intellectual property at Abbott Laboratories; and
- ***Sapna Srivastava, Ph.D., our Chief Financial and Strategy Officer***, who brings more than 13 years of financial and industry experience as a biotechnology analyst at Goldman Sachs & Co., Morgan Stanley and J.P. Morgan Chase & Co.

In addition, our founders and scientific advisors embody the core elements of our therapeutic approach, having experience with the CRISPR/Cas9 complex, delivery modalities and target diseases. They are considered to be some of the world's leading experts in CRISPR/Cas9 technology and in their respective fields. One of our co-founders, and a co-founder of Caribou Biosciences Inc., or Caribou, Dr. Jennifer Doudna, is widely recognized for her contributions to the development of CRISPR/Cas9 as a genome engineering tool. Additional members of our advisory team have made significant contributions to the understanding of CRISPR/Cas systems and help support the foundation we have today for developing human therapeutics based on gene editing technologies. Our founders are also currently active scientific advisors to the Company and include Dr. Doudna; Dr. Rodolphe Barrangou of North Carolina State University and chairman of the board of directors at Caribou, a pioneer in establishing the adaptive immune function of CRISPR systems; Dr. Rachel Haurwitz, chief executive officer of Caribou, who also serves on our board of directors; Dr. Andrew May, chief scientific officer of Caribou; Dr. Luciano Marraffini of Rockefeller University, a leader in the investigation of the underlying molecular mechanisms of CRISPR immunity; Dr. Derrick Rossi of Harvard Medical School, a hematopoietic stem cell expert; and Dr. Erik Sontheimer of the University of Massachusetts Medical School, an innovator in understanding the mechanism of CRISPR-mediated immunity in bacteria. All of these founder advisors are equity holders of our company and receive compensation as scientific advisors. Although they are regularly available for scientific consultation, our arrangements with these individuals do not entitle us to any of their existing or future intellectual property derived from their independent research or research with other third parties.

**Strategy**

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

***Focus on Sentinel 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 sentinel indications that have significant unmet medical needs based on four primary axes:

- 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 modalities.

We believe these selection criteria position us to build a risk-diversified pipeline, where 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 sentinel indications to inform our selection of subsequent indications and targets of interest. We believe this approach serves to increase the probabilities of success in our sentinel indications, generate insights that will accelerate the development of subsequent 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 sentinel *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. The first *in vivo* indications we are evaluating are ATTR, AATD, HBV and IEMs.

***Continue to Develop and Expand our* Ex Vivo *Therapeutic Programs.*** In collaboration with Novartis, we intend to rapidly develop the CAR T cell and HSC programs. We believe that our sentinel work in CAR T cells and HSCs will guide us in building a portfolio of additional proprietary *ex vivo* opportunities through our eXtellia division, including expanded immuno-oncology therapeutics beyond CAR T cells, such as modified NK cells and TILs, and autoimmune applications of Tregs, in addition to potential applications for other cell types such as induced pluripotent stem cells, mesenchymal stem cells and muscle satellite stem cells.

***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 potentially 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 expand our impact to broader patient populations. Our partnership focusing on CAR T cells with Novartis, an industry leader with one of the most advanced clinical CAR T cell programs, and our partnership with Regeneron, a leader in human genetics research, exemplify this strategy.

***Grow Our Leadership Position in the Field of Gene Editing.*** We are committed to broadening our capabilities to remain at the cutting edge of gene 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.

**Gene Editing**

Gene editing is the precise and targeted modification of the genetic material of cells. Gene editing works by using an enzyme to make a cut at a particular sequence in the genome, followed by deletions, repairs or insertions of genetic material at the cut site facilitated by the cell's natural DNA repair mechanisms. Coupled with recent advances, including a greater understanding of genetic diseases and maturation of gene therapy and associated delivery technologies, the development of gene editing tools that can permanently and precisely edit DNA may enable the development of therapies that can address, and potentially cure, the cause of DNA-based diseases.

Accordingly, we believe that gene editing has the potential to treat a broad range of diseases not adequately addressed by more traditional therapeutic modalities such as small molecules and biologics. Given its permanent effects on the target DNA in question, gene editing could potentially cure a disease with a single treatment course as opposed to the multi-treatment or chronic dosing regimens often seen with traditional modalities, which typically have transient effects and may require life-long treatment. Additionally, unlike gene therapy, which typically involves introducing a copy of a gene into a patient's cells, gene editing has the potential to make permanent, precise changes directly to the target gene in its normal location, repairing the underlying genetic mutation. This attribute may provide a significant competitive edge over gene therapy, as gene editing can yield a result close to or identical to the normal biological system in addition to addressing a broader spectrum of diseases.

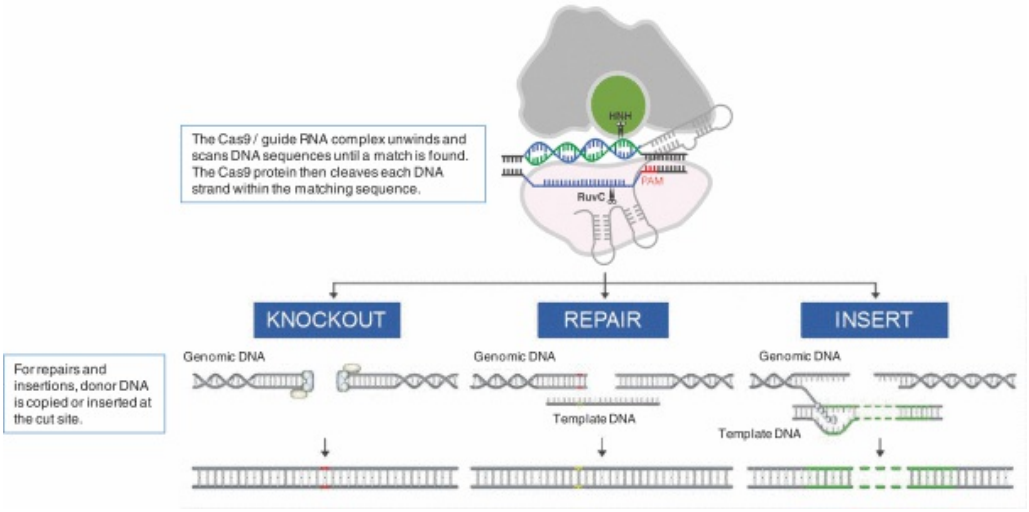
Earlier-generation gene editing methods such as zinc finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENs) use pairs of synthetic proteins engineered to recognize specific DNA sequences. While these systems have contributed to the clinical development and regulatory pathway for gene editing therapies, their development is relatively complex and costly because each synthetic protein may have variable cleavage activity and can be challenging and time consuming to manufacture because both proteins in the pair must be redesigned for each new target DNA sequence.

**About CRISPR/Cas9**

One of our co-founders and current scientific advisors, Dr. Rodolphe Barrangou, and other researchers originally characterized CRISPR/Cas systems as naturally occurring defense mechanisms in various bacterial species that protect against foreign DNA. In 2012, another 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 gene editing tool. Following Dr. Doudna's pioneering work, researchers were able to demonstrate the simplicity and versatility of the CRISPR/Cas9 system by quickly applying the system in a variety of contexts to better understand biological mechanisms and investigate disease models, resulting in more than 2,600 published papers since 2012.

Generally, CRISPR/Cas systems include one or more proteins that cleave DNA guided by an RNA guide sequence, pieces of RNA that both recognize specific DNA sequences and activate the cleaving activity of the Cas proteins. In the original bacterial systems, arrays of RNA sequences that recognize foreign DNA are sometimes referred to as clustered regularly interspaced short palindromic repeats, or CRISPRs, while certain proteins have been named as numbered CRISPR associated, or Cas, proteins. Currently, the simplest and most versatile type of CRISPR/Cas system uses the Cas9 protein as the DNA cutting enzyme, as described in Dr. Doudna's seminal paper.

Two basic components of the CRISPR/Cas9 gene editing system are the Cas9 protein and a guide RNA sequence that recognizes and directs the Cas9 to a specific target DNA sequence. The system edits DNA as follows:




Because an RNA sequence complementary to any DNA sequence can be rapidly designed and synthesized, a CRISPR/Cas9 system can be efficiently and specifically reprogrammed by changing only the guide RNA sequence, without any need to modify the cutting protein. The simplicity of programming the CRISPR/Cas9 system, coupled with its efficiency and flexibility, opens the door to a wide range of *in vivo* and *ex vivo* therapeutic applications, including the potential to apply an approach in which multiple genes are edited simultaneously to target more complex multi-gene or polygenic disorders.

We believe that CRISPR/Cas9 offers significant potential benefits over other gene editing methods, including:

- higher selectivity and cleavage efficiency;
- simpler tools allowing for rapid scaling and optimization;
- more efficient path to achieve preclinical proof-of-concept;

- broader applicability to *in vivo* and *ex vivo* therapies;
- greater potential for single curative treatment; and
- greater potential to address polygenic or complex genetic disorders by targeting multiple DNA sites simultaneously.

The CRISPR/Cas9 system allows us to make three general types of edits: knockouts, repairs and insertions. Different diseases can be addressed using one or more of these editing strategies, depending on the particular genetic defect and the spectrum of genetic defects within a patient population.

| Type of Edit | Description | Mechanism of Action | Application | Example Indications |
|---|---|---|---|---|
| Knockout | • Edits that cause loss of function<br>• Can be applied to genes that make harmful proteins or disease-causing viruses | CRISPR/Cas9 engineered to make:<br>• A single cut in a gene to promote addition or deletion of short pieces of DNA, or two cuts in close proximity to delete a fragment of DNA<br>• As a result, the gene is disrupted and the protein is either not made or is non-functional | • Autosomal dominant disorders<br>• Infectious diseases | • Transthyretin amyloidosis<br>• Alpha-1 Antitrypsin Deficiency<br>• Hepatitis B Virus<br>• Inborn Error of Metabolism, such as Primary Hyperoxaluria Type 1, or PH1 |
| Repair | • Edits that repair disease-associated gene mutation(s)<br>• Can be applied to single point mutation or mutations restricted to a small region of DNA | CRISPR/Cas9 engineered to make:<br>• At least one cut at the target site, delivered with a short, single-stranded DNA donor template containing the correct sequence<br>• Cell repairs DNA break by filling in the gap with the corrected sequence from the donor template<br>• Results in expression of the corrected protein | • Any genetic mutation | • Alpha-1 Antitrypsin Deficiency<br>• Several Inborn Errors of Metabolism |
| Insertion | • Edits that correct a disease-associated gene<br>• Can be applied to insert a functional gene or replace part of a gene where mutations are distributed across a large region of DNA | CRISPR/Cas9 engineered to make:<br>• At least one cut at the target site, delivered with a large, double-stranded DNA donor template containing the correct sequence<br>• Cell repairs DNA break by inserting the donor sequence<br>• Results in expression of the corrected or functional protein | • Protein expression<br>• Insertion of wild-type protein | • Several Inborn Errors of Metabolism, including Phenylketonuria, or PKU |

**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 are actively developing robust, high volume, or 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.

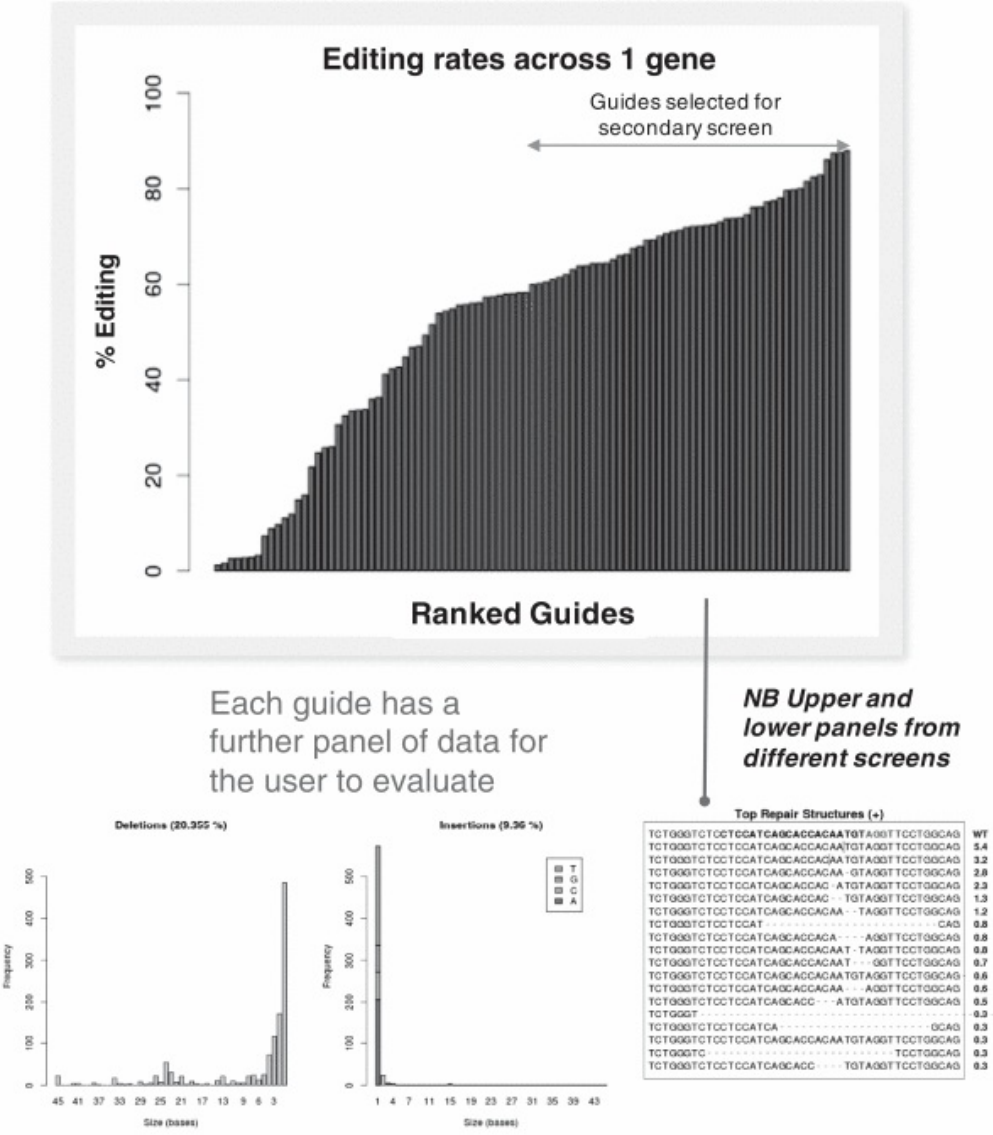
*Informatics*

We are building a high-throughput, scalable data processing and analysis, or informatics, infrastructure to support various aspects of our platform, including guide 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 intend 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 evaluate the ability of numerous guide RNAs to generate the required edit at the genomic site of interest, called on-target activity, as well as their propensity to generate unwanted events at other sites in the genome, also known as off-target activity. To assess 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. In the figure below, the top panel shows the ranking of representative screened

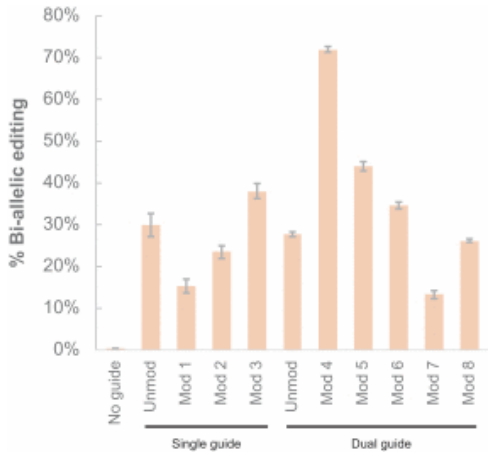
guides by editing efficiency, while the bottom panels show the specific types of edits and the resulting edited sequences. These data enable us to select the most attractive candidate guides to effect the desired on-target edit.




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 candidate 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 improve our guide RNA qualification capability over time by increasing our throughput, advancing 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 improve editing efficiency and reduce the likelihood of an immune response. As indicated in the figure below, structural and chemical modifications of a guide targeting the same sequence can have a significant impact on editing rates, demonstrated by the percentage of cells having both copies of the target DNA sequence knocked out, which is referred to as bi-allelic editing. 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*, or *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 activity and manufacturability. In addition, we are exploring other naturally-occurring Cas9 proteins from other organisms, which may differ from *Spy* Cas9 in aspects such as specificity or size. We are pursuing these alternative Cas9 forms through ongoing internal work, by collaborating with our scientific founders and by investigating in-licensing opportunities. We are also investigating altered versions 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, depending on the target cell or tissue of interest, the delivery method and the desired type of edit.

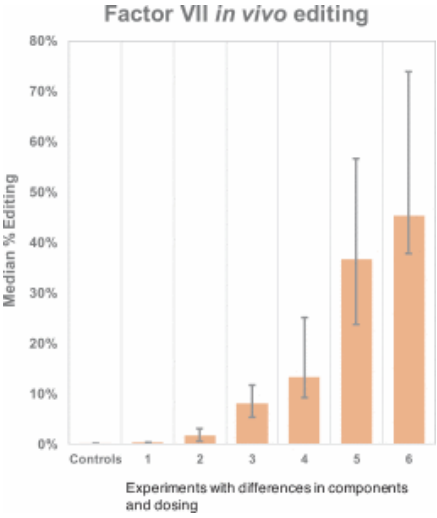
*Edit type*

While knockout type edits can be made using only a Cas9 protein and guide RNA, repair and insertion type 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 type edits. To date, we have observed up to 20% repair type edits in an *ex vivo* setting by administering CRISPR/Cas9 and repair templates to primary cells.

*In vivo delivery*

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

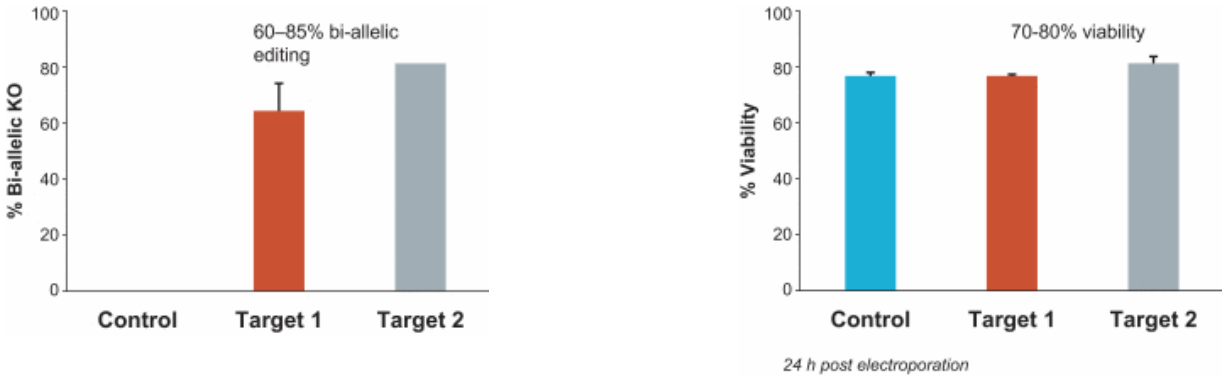
LNPs encapsulate the therapeutic material, providing it with stability, improved pharmacologic properties and controlled circulation time, allowing for transient expression of Cas9. We see multiple advantages of using LNPs as our initial *in vivo* delivery vehicles, particularly as optimized by us for delivery of the CRISPR/Cas9 system. Certain LNPs have demonstrated efficacy, safety and favorable tolerability and are currently used as a delivery system for therapeutic small interfering RNA, or siRNA, as well as therapeutic messenger RNA, or 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 in the clinic, with the most advanced in Phase III development. For CRISPR/Cas9-based therapies, where potentially only one or few treatment courses are needed, LNPs have 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 were developed by and in-licensed from Novartis for use with CRISPR/Cas9 products. To date, we have successfully demonstrated *in vivo* editing in mouse liver with a single dose of systemically delivered LNPs based on these lipids. The figure below shows editing of a surrogate target, Factor VII, with editing efficiencies varying depending on the specific formulation and components, as well as dosing regimens.



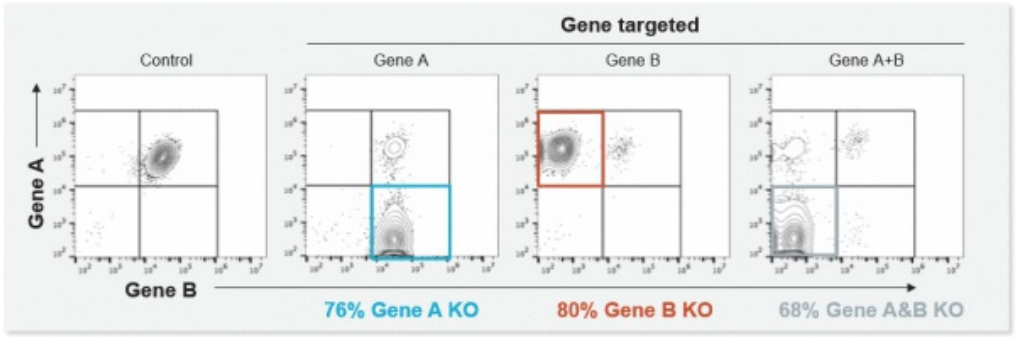

With our team's expertise in LNP delivery technology, we expect to be able to translate the LNPs that we are using for our preclinical evaluation to clinical development in humans. In addition, we are exploring options for incorporating Cas9 into therapeutic products in multiple formats. For example, Cas9 can be delivered in its protein form or could be delivered by a nucleic acid, such as an mRNA or a viral vector. 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 optimize LNP formats for a variety of CRISPR/Cas9 therapeutic components, including templates for repair and insertion type 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 and other organs.

*Ex vivo delivery*

Our *ex vivo* delivery approach is a clinically proven delivery 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 in delivery efficiency or cell viability. In human cells, we have been able to achieve relatively high editing rates of both copies of a single gene, or bi-allelic editing, while preserving cell viability as indicated in the figure below.




We have also simultaneously targeted multiple genes with high bi-allelic editing rates for both genes, demonstrating what we believe to be therapeutically relevant editing of multiple genes simultaneously, or multiplex editing, in an *ex vivo* setting as shown in the figure below. We believe that the ability to achieve multiplex editing may be critical in targeting certain diseases.




*Guides are from different genes. CD3⁺ primary T cells. Electroporated RNP (n=3); one replicate shown*

**Our Pipeline**

To accelerate the development and commercialization of CRISPR/Cas9-based products in multiple therapeutic areas, we are targeting sentinel 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 sentinel *in vivo* indications initially target chronic liver diseases, including ATTR, AATD, HBV and IEMs. Our initial efforts on *in vivo* delivery focus on the use of LNPs for delivery of the CRISPR/Cas9 complex to the liver.

*Transthyretin Amyloidosis Program (Knockout Strategy)*

Transthyretin is a protein produced primarily in the liver, encoded by the *TTR* gene. This protein carries retinol, or vitamin A, and thyroxine, or 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, or ATTR. Over 120 different 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, or FAP, whereas those leading to heart disease cause a syndrome called familial amyloidotic cardiomyopathy, or FAC. Ongoing amyloid deposition in tissues due to disease progression results in the development of cardiomyopathy and other cardiac symptoms observed in FAC patents. Typical onset of disease symptoms occurs around 20-70 years of age and can be fatal within two to 15 years. Estimates suggest that approximately 50,000 patients suffer from ATTR worldwide.

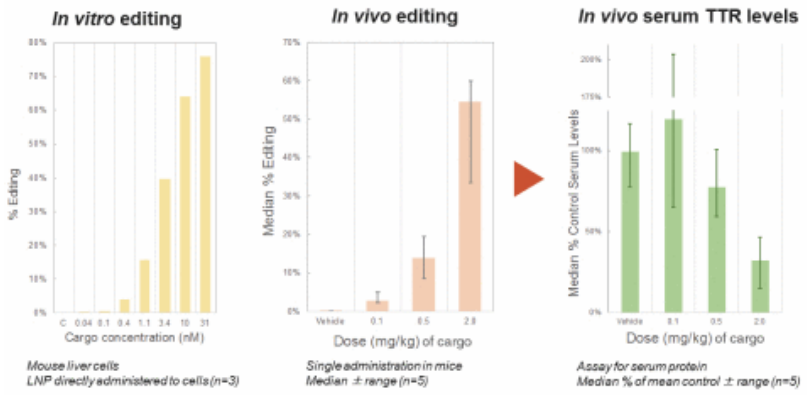
Limitations of Current Treatment Options

Treatment options for ATTR are severely limited and largely ineffective. In advanced cases of FAP, liver transplants can be used to eliminate the source of mutant protein production; however, in a subset of transplanted patients, normal TTR continues to aggregate on existing amyloid deposits resulting in continued disease progression, which results in increased mortality in patients with cardiac symptoms. For FAC patients, the primary therapy involves treatments to prevent heart failure; however, the prognosis for these patients is poor, with an average life expectancy of approximately two to four years from diagnosis.

Our Solution

We believe that we can apply CRISPR/Cas9 technology to potentially cure ATTR by knocking out expression of the defective *TTR* gene in the liver. We expect this approach to greatly reduce or eliminate the production of the disease-causing mutant form 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 reduction and clinical benefit. Additionally, these studies suggest that loss of *TTR* expression from the liver would be well-tolerated in adult humans. Accordingly, we believe targeting mutant *TTR* with CRISPR/Cas9 may improve patient outcomes by potentially eliminating mutant *TTR* gene expression in a single or small number of treatments, as opposed to life-long therapy. We have begun to assess

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 mice after a single intravenous administration, as indicated in the figure below.




Clinical Development Pathway

Our first in-human studies in ATTR will take place in a small number of 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 mutant TTR protein as well as decreases in amyloid plaques within target tissues. We also plan to assess liver, kidney, heart, and nerve function. We expect that the results of our preclinical studies, and discussions with the FDA, EMA and 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 and Repair Strategies)*

AATD is an inherited genetic disorder that may cause lung or liver disease. The lung disease may result in chronic obstructive pulmonary disease, or 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, or 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 cells, or 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 patients, 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.

Limitations of Current Treatment Options

There is currently no cure for AATD. The most common form of treatment for AATD-related lung disease is intravenous augmentation therapy, or plasma protein replacement therapy, where patients are infused with donor plasma proteins enriched for AAT. The goal of this treatment is to increase the levels of AAT circulating

in the body to protect lung tissue from neutrophil elastase. Patients are infused weekly and require life-long treatment. The infused proteins slow, but do not cure, the pulmonary pathology. Existing treatment options also include standard forms of therapy for COPD, such as bronchodilators, anti-inflammatory agents and antibiotics, which only address disease symptoms. None of these treatments address the hepatic form of the disease, where in the most severe cases, liver transplantation may be needed.

Our Solution

We believe that we can apply the CRISPR/Cas9 technology to cure AATD by addressing the defective *SERPINA1* gene. We intend to evaluate two editing approaches—a knockout and a 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 will be treated with plasma protein supplementation to achieve levels of the normal form of AAT to be active against the lung disease. Appropriate guide RNA selection will be important for achieving this knockout with high specificity and high efficiency.

We believe our repair approach for AATD will address the lung disease as well as the liver disease. With this strategy, we intend to 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 this correction will 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 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 repair of only a limited number of hepatocytes might be sufficient to address this disease. We expect the progress of this program 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 both of our knockout and repair programs in clinical development.

Clinical Development Pathway

For both our knockout and repair strategies, our first in-human studies will take place in a small number of 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, other global regulatory agencies and the AATD community will be important for selecting the appropriate patients and endpoints for our clinical trials.

*Hepatitis B Virus Program (Knockout Strategy)*

Hepatitis B is an infection of the liver caused by HBV which 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.

Limitations of Current Treatment Options

We believe there is a clear unmet need for patients with chronic HBV. The current treatment options, which include interferons and nucleos(t)ide analogs, primarily control viral replication but rarely eradicate the virus.

Additionally, different genotypes of HBV have variable responses to existing treatments. In the United States, despite the large pool of diagnosed HBV patients, many patients do not receive treatment. Current treatments are typically life-long with risks of long-term side effects.

The persistence of chronic HBV results from a form of the virus that is found in the host nucleus known as cccDNA, which serves as a template for viral replication. It also acts as a reservoir of the virus, which can become reactivated and re-infect that patient. Clinical evidence suggests that the presence of cccDNA is a significant reason that HBV cannot be eliminated in most patients. There are currently no approved therapies that specifically eradicate cccDNA from infected patients.

Our Solution

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. 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 believe it is also possible that a common treatment solution can be developed for all genotypes of HBV because we can target 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 intend to evaluate different knockout approaches to eliminate cccDNA *in vivo*, including cleaving the cccDNA in various individual or a combination of locations.

We have completed a bioinformatic analysis of potential CRISPR/Cas9 target sites in the HBV genome to select a set of guide RNAs, including several which can be effective across all HBV genotypes. We have identified potential CRISPR/Cas9 target sites by examining the known sequences of HBV isolated from patients. We plan to use a cell line that produces infectious HBV particles as well as cccDNA to identify lead guide RNAs. The lead guide RNAs will then be assessed for their ability to prevent infection and propagation of HBV, and evaluated for off-target effects, in both cell and animal models of HBV.

Clinical Development Pathway

We expect our expected clinical development path to indicate evidence of safety and antiviral activity in patients infected with HBV. The key objective of this study 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 U.S. Food and Drug Administration, or FDA, other global regulatory agencies and the HBV community, will be important for selecting the appropriate patients and endpoints for our clinical trials.

*Inborn Errors of Metabolism, or 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 are evaluating a large set of candidate IEMs, including primary hyperoxaluria type 1, or PH1, argininosuccinic lyase deficiency, ornithine transcarbamylase deficiency, phenylketonuria, or PKU, and maple syrup urine disease. Our selection criteria for our initial 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.

**Ex Vivo *Pipeline***

Our sentinel *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. Our *ex vivo* programs will help inform the broader applicability of CRISPR/Cas9 in other relevant types of immune cells, such as NK cells and TILs, in addition to potential applications in other cell types such as induced pluripotent stem cells, mesenchymal stem cells and muscle satellite stem cells.

For our *ex vivo* programs requiring delivery to extracted cells such as HSCs or T cells, 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*, such as membrane disruption via mechanical forces or modified chemical compositions outside the cells, which may provide advantages in delivery efficiency or cell viability.

*CAR T Cell Program*

CAR T cell therapies are currently being developed for blood cancers such as acute lymphoblastic leukemia, or ALL, acute myeloid leukemia, multiple myeloma and chronic lymphocytic leukemia. In CAR T cell therapy, naturally-occurring immune cells, specifically T cells, are modified *ex vivo* by inserting a chimeric antigen receptor, or CAR, into the T cells, thereby activating an immune response against cancer cells. CAR T cell products, including Novartis' CAR T cell candidate, CTL019, have shown clinical promise in addressing hematological malignancies such as ALL. While existing CAR T cell products have shown great clinical promise, they 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 modulate pathways in T cells to enhance their survival or activity against cancer cells.
- CRISPR/Cas9 could be used to introduce the CAR into a precise location, 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 three common classes of blood-related disorders: hemoglobin disorders, such as 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 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 by employing a proprietary small molecule for HSC expansion to which Novartis has granted us rights. This small molecule could allow us to generate large 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 selection. 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. We expect the first investigational new drug application for an HSC program under the Novartis collaboration to be submitted by Novartis in 2018.

*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. For more information regarding our ongoing collaboration with Novartis, see the section entitled "—Collaborations—Novartis Institutes for BioMedical Research, Inc." appearing elsewhere in this prospectus for more information.

***Future Development Opportunities***

We believe our sentinel indications will provide us with broad experience across a variety of gene editing strategies that we can apply to selecting future therapeutic opportunities.

*In Vivo*

Future indications requiring delivery to tissues in organs beyond the liver, such as the eye, muscle or central nervous system, will require more research and development work, including around next generation delivery methods. As we progress our sentinel liver programs, we are actively investigating additional delivery methods, including evaluating multiple viral delivery vectors that may allow us to explore therapies for indications in additional tissues. One viral vector that we are evaluating, adeno-associated virus, or AAV, is already utilized in a gene therapy product approved in the European Union, or EU. While AAV has enough capacity to deliver a Cas9 protein and guide RNA, a second vector would be required for applications involving a larger DNA repair template. We believe that using a multi-vector system is feasible for effecting more complex repairs; however, we are also exploring alternative viral delivery systems including larger capacity vectors based on adenovirus, lentivirus and herpes simplex virus. In certain cases, these viral vectors can be modified to deliver nucleic acid material to specific cells or tissue types, allowing for customized delivery of CRISPR/Cas9 components to the cells needing repair. Given the variety of possible genetic targets for CRISPR/Cas9, we are currently evaluating the technologies of several academic groups and companies with expertise in various delivery systems to determine the best delivery vehicle for different therapeutic indications. In choosing a delivery vehicle for a particular application, we will consider factors including capacity, delivery specificity and efficiency, clinical safety, immunogenicity and manufacturing ability. Internally, we are developing CRISPR/Cas9 components and systems that we believe can be easily adapted to multiple delivery systems.

*Ex Vivo*

We expect that our experience in CAR T cells will guide us in building a portfolio of additional *ex vivo* opportunities through our eXtellia division, enabling us to expand the application of CRISPR/Cas9 for immuno-

oncology therapeutics beyond CAR T cells, including to tumor-infiltrating lymphocytes, or TILs, cytotoxic T lymphocytes, or CTLs, and CAR-engineered natural killer cells, or CAR-NKs. The field of immuno-oncology is still emerging and rapidly developing. Immunologists continue to gain key insights about the regulation of the immune system, the role of different cell types that elicit the immune response, pathways that govern the survival of cells and methods to manipulate cells for therapeutic purposes. We plan to apply this information to further expand our efforts in oncology, both solid and hematological, or liquid, tumors and believe we can gain the following benefits from our application of CRISPR/Cas9 to these immuno-oncology therapeutics:

- enhanced efficacy by receptor engineering;
- enhanced potency by checkpoint engineering;
- enhanced safety by applying kill switches; and
- simplified manufacturing by creating allogenic products requiring non-viral manufacturing.

We believe that we can further apply the experience we gain in immuno-oncology to autoimmune diseases, which result from the immune system recognizing a patient's own cells or proteins as foreign to the body. Autoimmune diseases can arise when Tregs have insufficient activity. Gene editing may be used to increase the activity of Tregs by targeting certain regulatory proteins, which we believe will enhance efficacy by improving homing to the target tissue and enhance potency by improving suppressor function.

While our initial focus is on CAR T cells and HSCs, under our Novartis collaboration, and immuno-oncology and autoimmune and inflammatory diseases under our eXtellia division, we plan to explore in eXtellia other cell types where we believe we can effectively apply CRISPR/Cas9 technology, such as pluripotent stem cells, mesenchymal stem cells and muscle satellite stem cells. We believe that we can apply CRISPR/Cas9 to modify these cells to produce therapeutically relevant proteins for the treatment of systemic disease upon reimplantation of the modified cells into patients. Advances in delivery technologies and CRISPR/Cas9 platform optimizations made through our sentinel *ex vivo* programs will facilitate development of any of these subsequent programs.

**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 and license agreement with Novartis, 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 platform in HSCs and CAR T cells. The collaboration is also governed by research plans for each of the HSC and CAR T cell programs that outline the parties' responsibilities under, anticipated timelines of and budgets for the programs, and is overseen by a joint steering committee, or JSC, formed by representatives from us and Novartis. Among other activities, the JSC reviews the collaboration program and forms subcommittees to evaluate and nominate the pool of potential research targets under and approve the research plans for the HSC and CAR T cell programs.

Within the HSC therapeutic space, Novartis may obtain exclusive rights to a limited number of HSC targets, to be chosen by Novartis in multiple 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 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 JSC. After completion of the research 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 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 the 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 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 their 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 an existing out-license of our CRISPR/Cas9 platform to a third party; and (iii) are not the subject of ongoing or planned research and development by us.

During the collaboration term, with respect to the HSC and CAR T cell programs, and for as long as the applicable party continues to use commercially reasonable efforts to research, develop and commercialize the HSC, CAR T cell and *in vivo* products contemplated by the agreement, neither party may collaborate with a third party with regard to the activities contemplated by the HSC, CAR T cell or *in vivo* programs nor grant licenses to practice such party's intellectual property licensed under the agreement in the selected HSC or CAR T cell or *in vivo* field to a third party. Following the collaboration term, if Novartis fails to comply with its obligation to research, develop and commercialize at least one HSC or CAR T cell product, we will have the right to terminate Novartis' exclusive rights with respect to the selected HSC or CAR T cell target and terminate Novartis' license to practice our intellectual property licensed under the agreement in such applicable target.

Under the agreement, we received an upfront technology access payment of $10.0 million and are entitled to an additional $40.0 million, in the aggregate, in additional technology access fees and research payments during the five-year collaboration term. In addition, for each product under the collaboration, 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 U.S. and the 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. In addition, Novartis will reimburse us for all royalty payments owed by us as a result of its sales under the intellectual property we license from Caribou.

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 for the purposes of performing activities contemplated by the collaboration. Our license grant to Novartis of our CRISPR/Cas9 platform technology, including a sublicense to certain platform rights licensed from 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 developed out of the collaboration related to our CRISPR/Cas9 platform will be owned solely by us, while all other intellectual property developed out of 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. Novartis may terminate the agreement if the owners or licensees of U.S. patent 8,697,359 bring a suit against Novartis on or before December 31, 2017 claiming that the activities specifically contemplated by the collaboration research plans infringe an independent claim of such patent. 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 have the ability to 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 will be focused in the liver.

We retain the exclusive right to solely develop products for our sentinel liver indications, other than ATTR, which are the "Reserved Targets." ATTR, the first target selected by Regeneron, is subject to a co-development and co-commercialization arrangement between us and Regeneron. 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. 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.

A joint steering committee consisting of an equal number of representatives from us and Regeneron will oversee the general strategies and activities undertaken by the parties under the collaboration. Research activities under the collaboration will be governed by evaluation and research and development plans that will outline the parties' responsibilities under, anticipated timelines of and budgets for, the various programs. 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 the joint steering committee. We may assist, as requested by Regeneron, with the later discovery and research of product candidates directed to any 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.

We may research, develop, manufacture or commercialize products for our Reserved Targets, on our own or in collaboration with a third party. During the collaboration term, we, on our own or in collaboration with a third party, may not research, develop, manufacture or commercialize a liver target that is subject to a Regeneron co-development and co-commercialization option or that Regeneron may potentially select through the target selection process.

In connection with this collaboration, Regeneron agreed to purchase $50.0 million of our common stock in a private placement, and we received a nonrefundable upfront payment of $75.0 million. In addition, we are eligible to earn, on a per-licensed target basis, up to $25.0 million, $110.0 million and $185.0 million in development, regulatory and sales-based milestone payments, respectively. We are also eligible to earn royalties ranging from the high single digits to low teens, in each case, on a per-product basis, which royalties are potentially subject to various reductions and offsets and are further subject to our existing low single-digit royalty obligations under our Caribou license agreement.

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 expand our impact to broader patient populations. In forming these partnerships, we believe we will be able to more rapidly expand our impact to broader patient populations.

**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 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 Biosciences, Inc., or 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 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 includes exclusive rights in our field of use to any CRISPR/Cas9-related intellectual property developed by Caribou between July 16, 2014 and, at least, July 16, 2016. 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 owned by The Regents of the University of California and the University of Vienna, 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 are also receiving two years of research and development services from Caribou. Under the services agreement's research plan, Caribou primarily focuses on the improvement and further development of the CRISPR/Cas9 system and its components. 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 are paying 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 $1.1 million paid through December 31, 2015. 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, at least, July 16, 2016. 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, as well as intellectual property from Wageningen University. Further, under the license agreement, we have an option to sublicense for our field of use any new intellectual property in-licensed by Caribou through, at least, July 16, 2016. 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 40 patent applications in the United States and internationally that 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 IP*

The Regents of the University of California and the University of Vienna, which we collectively refer to as UC/Vienna, co-own a worldwide patent portfolio with Dr. Emmanuelle Charpentier 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 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 March 31, 2016, this family does not yet contain any issued patents in the United States, but claims in one U.S. patent application have been found allowable pending interference proceedings described elsewhere in this prospectus. 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 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. In certain jurisdictions outside the United States, such as Canada and countries in the EU, there are various limitations on or conditions to the ability of one co-owner to use, assign, license or enforce its patent rights without the consent of all other co-owners. Accordingly, because we do not yet have Dr. Charpentier's consent to our sublicense of the UC/Vienna intellectual property, we may be subject to these limitations in the applicable foreign jurisdictions. In addition, any co-owner from whom we do not yet have a license may raise claims surrounding inventorship or ownership of patents that ultimately issue from this patent family, potentially resulting in issued patents to which we would not have rights our existing license. For products covered by this license and their companion diagnostics, we will owe low 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, we would become UC/Vienna's direct licensee instead of Caribou.

On April 13, 2015, UC/Vienna and Dr. Charpentier jointly filed a request with the United States Patent and Trademarks Office, or USPTO, asking that an interference be declared between the 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, which we collectively refer to as the Broad Institute patent family, that 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, or PTAB, of the USPTO declared an interference involving one UC/Vienna/Charpentier application, 12 Broad issued patents and a Broad patent application. The USPTO named the UC/Vienna/Charpentier group as the senior party in the interference. In an interference proceeding, the senior party is presumed to be the first inventor, while the junior party has the burden of proving earlier invention. The initial motions phase of this proceeding may last approximately one year or more. The PTAB could take up to 24 months or more to render a final decision, and its decision may subsequently be appealed to the U.S. Court of Appeals for the Federal Circuit. We cannot guarantee that UC/Vienna and Dr. Charpentier will prevail in the interference proceeding or obtain issued claims generally covering the use of the CRISPR/Cas9 gene editing system in humans.

*Pioneer Hi-Bred International (DuPont Company) IP*

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 sublicense is worldwide and royalty-free, with a one-time $0.6 million aggregate milestone payment for activities through Phase III clinical trials for a first therapeutic product and $0.5 million to $1.0 million for each of the first three new drug applications or biologics license applications filed.

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. Any patents obtained from this family will expire in or after 2033, assuming payment of necessary maintenance fees. We cannot ensure that these applications will lead to issued claims that cover our products or activities.

*Wageningen University IP*

Our license agreement with Caribou also includes exclusive access to a patent family from the Wageningen University relating to CRISPR/Cas systems, which has been assigned from Wageningen University to Caribou. The family claims priority to a December 30, 2011 application, which discloses various Cas proteins and CRISPR/Cas systems. If we develop and sell a product covered by issued patents in this family, we will owe royalties to each of Wageningen University and Caribou of less than one percent on net sales. We cannot be certain whether patents will issue from these applications that cover our products.

***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 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 out of 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 plan to rely on 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 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 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 gene 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, we will 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:

- gene editing companies focused on CRISPR/Cas9 including: CRISPR Therapeutics, Inc., Editas Medicine, Inc. and Tracr Hematology Limited;
- other gene editing companies including: bluebird bio, Inc., Cellectis S.A., Poseida, Inc., Precision BioSciences, Inc., and Sangamo BioSciences, and
- gene therapy companies developing *ex vivo* therapies including: bluebird bio, Inc., Cellectis S.A., and Juno Therapeutics, Inc.

Our competitors will also include companies that are or will be developing other gene editing methods as well as small molecules, biologics 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 product candidates to be regulated as biologics. Biological products are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and the Public Health Service Act, or 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 biological products. Before clinical testing of biological products in the United States may begin, we must submit an investigational new drug application, or IND, to the FDA, which reviews the clinical protocol, and the IND must become effective before clinical trials may begin. In some instances, we must also submit our protocols to the National Institutes of Health, or NIH, through its Recombinant DNA Advisory Committee, or RAC, for review before initiating clinical testing.

Biologic products must be approved by the FDA before they may be legally marketed in the United States 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, or CBER, regulates biologic products. 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 testing, and chemistry, manufacturing and control information in gene therapy INDs.

Although the FDA has not yet approved any human gene therapy product for sale, it has provided guidance for the development of gene therapy products which may be relevant to gene editing products as well. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies, or OCTGT, within CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee, or CTGTAC, to advise CBER on its reviews. In addition, the FDA has issued a growing body of clinical, chemistry, manufacturing and control, or CMC, guidance and other guidance, all of which are intended to facilitate industry's development of gene therapy products. In 2012, the European Medicines Agency approved a gene therapy product called Glybera, which is the first gene therapy product approved by regulatory authorities anywhere in the Western world.

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. Biological Products Development Process***

The FDA approves biologics through the Biologics License Application, or BLA, process before they may be legally marketed in the United States. 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, or 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, or 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 biological product for its intended use;
- submission to the FDA of a BLA for marketing approval that includes substantive evidence of safety, purity, and potency from results of nonclinical testing and clinical trials;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with current Good Manufacturing Practice, or cGMP, to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity and, if applicable, the FDA's current good tissue practice, or 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 BLA; and
- FDA review and approval, or licensure, of the BLA.

Before testing any 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, or OBA, pursuant to the NIH Guidelines for Research Involving Recombinant DNA Molecules, or 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 at one of its quarterly public meetings. 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 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 suspend or terminate such trials.

Clinical trials involve the administration of the biological 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, or 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, or IBC, a local institutional committee that reviews and 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 biological 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 biological 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, 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 recommends 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 results 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 biological 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 biologics, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss 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.

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, purity and potency of human gene editing products, 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 biological product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP 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 biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological 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 biological product candidate, FDA approval of a BLA must be obtained before commercial marketing of the biological product. The 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, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological 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, or 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, or 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 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 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, or PDUFA, as amended, each BLA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's fee schedule, effective through September 30, 2016, the user fee for an application requiring clinical data, such as a BLA, is $2,374,200. PDUFA also imposes an annual product fee for biologics ($114,450) and an annual establishment fee ($585,200) on facilities used to manufacture prescription biologics. 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 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 a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA 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 BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe and potent, or effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with cGMP requirements to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biological products or biological 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 biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the biological product candidate. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a 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 a 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 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 BLA in its present form, the FDA will issue a complete response letter that usually describes all of the specific deficiencies in the BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring 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 BLA, 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 and dosages 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 or precautions 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 biological 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 standard BLAs in 10 months from the filing date and 90% of priority BLAs in six months from the 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 from time to time. 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 intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and marketing the drug for this type of disease or condition will be recovered from sales in the United States. Orphan product designation must be requested before submitting a 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 United States, 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 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 and then used off-label. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same biological product as defined by the FDA 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 biological products that meet certain criteria. Specifically, new 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 biologic may request that the FDA designate the biologic as a Fast Track product at any time during the clinical development of the product, but ideally not later than the 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 biological product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. 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 biological 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. Fast Track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

In addition, under the provisions of the Food and Drug Administration Safety and Innovation Act of 2012, or 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 meets the conditions for qualification. In addition, these designations may not provide us with a material commercial advantage.

***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 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 any 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 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 must 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 marketing of a product 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.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved 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 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 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 a BLA plus the time between the submission date of a 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 biological 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 U.S. PTO, 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 BLA. However, there can be no assurance that any such extension will be granted to us.

***Biosimilars and Exclusivity***

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or 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, or BPCIA, which created an

abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. To date, only one biosimilar has been licensed under the BPCIA, although numerous biosimilars have been approved in Europe. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trials or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity, or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the "first licensure" of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

During the 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The BPCIA is complex and only beginning to be interpreted and implemented by the FDA. In addition, recent government proposals have 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, 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.

***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 United States, 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.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical studies or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical study application much like the IND prior to the commencement of human clinical studies.

The requirements and process governing the conduct of clinical studies, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Similar to the United States, the various phases of pre-clinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the Member State regimes. To improve the current system, a new Regulation No. 536/2014 on clinical trials on medicinal product candidates for human use, which will repeal Directive 2001/20/EC, was adopted on April 16, 2014 and published in the European Official Journal on May 27, 2014. The new Regulation aims at harmonizing and streamlining the clinical trials authorization process, simplifying adverse event reporting procedures, improving the supervision of clinical trials, and increasing their transparency. The new Regulation entered into force on June 16, 2014 but will apply not earlier than May 28, 2016. Until then the Clinical Trials Directive 2001/20/EC will continue to apply. In addition, the transitional provisions of the new Regulation offer, under certain conditions, the clinical trial sponsors the possibility to choose between the requirements of the Directive and the Regulation for a limited amount of time.

Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU Member States where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions, or SUSARs, to the investigational product that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

In the EU, gene therapy medicinal products can only be commercialized after obtaining a Community Marketing Authorization, or Community MA. The Community MA is issued by the European Commission through the so-called Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and which is valid throughout the entire

territory of the EU. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is also mandatory for so-called Advance Therapy Medicinal Products (or ATMPs). ATMPs comprise gene therapy, somatic cell and tissue engineered products. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EU as of November 20, 2005, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

Under the Centralized Procedure, the CHMP serves as the scientific committee that renders opinions about the safety, efficacy and quality of human products on behalf of the EMA. The CHMP is composed of experts nominated by each Member State's national drug authority, with one of them appointed to act as Rapporteur for the co-ordination of the evaluation with the possible assistance of a further member of the Committee acting as a Co-Rapporteur. The CHMP has 210 days to adopt an opinion as to whether a marketing authorization should be granted. The process usually takes longer as additional information is requested, which triggers clock-stops in the procedural timelines. Based on the CHMP's opinion the European Commission will adopt a decision on the granting of the marketing authorization. In case of ATMPs, the EMA's Committee for Advanced Therapies, a multidisciplinary committee of experts on ATMPs, will prepare a draft opinion that will be submitted to the CHMP before the latter adopts its final opinion. Under the above described procedure, before granting the MA, the EMA makes an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

In the EU, new products authorized for marketing (i.e., reference products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic applicant from commercializing its product in the EU until ten years have elapsed from the initial authorization of the reference product in the EU. The ten-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications, which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

The EU also provides other opportunities for market exclusivity. For example, products receiving orphan designation in the EU can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product can also obtain an additional two years of market exclusivity in the EU for pediatric studies.

The criteria for designating an "orphan medicinal product" in the European Union are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan drug designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- The second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- The applicant consents to a second orphan medicinal product application; or
- The applicant cannot supply enough orphan medicinal product.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

***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.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, collectively the Affordable Care Act, to a stricter standard such that a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. The majority of states also have anti-kickback laws, which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers.

The federal false claims and civil monetary penalties laws, including the civil False Claims Act, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false, fictitious or fraudulent claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Actions under the civil False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the civil False Claims Act can result in very significant monetary

penalties and treble damages. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved (e.g., off-label) uses. In addition, the civil monetary penalties statute imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Many states also have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Given the significant size of actual and potential settlements, it is expected that the government authorities will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, the Affordable Care Act broadened the reach of certain criminal healthcare fraud statutes created under HIPAA by amending the intent requirement such that a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and certain other healthcare providers. The Affordable Care Act imposed, among other things, new annual reporting requirements through the Physician Payment Sunshine Act for covered manufacturers for certain payments and "transfers of value" provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties of up to an aggregate of $150,000 per year and up to an aggregate of $1 million per year for "knowing failures." Covered manufacturers were required to begin collecting data on August 1, 2013 and submit reports on aggregate payment data to the government for the first reporting period (August 1, 2013 – December 31, 2013) by March 31, 2014, and were required to report detailed payment data for the first reporting period and submit legal attestation to the completeness and accuracy of such data by June 30, 2014. Thereafter, covered manufacturers must submit reports by the 90th day of each subsequent calendar year. In addition, certain states require implementation of compliance programs and compliance with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, impose restrictions on marketing practices, or tracking and reporting of gifts, compensation and other remuneration or items of value provided to physicians and other healthcare professionals and entities.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or 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.

***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 United States 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, 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.

***Healthcare Reform***

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of

reimbursement for particular medical products. By way of example, in the United States, the Medicare Prescription Drug Improvement and Modernization Act of 2003, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for outpatient drug purchases by those covered by Medicare under a new Part D and introduced a new reimbursement methodology based on average sales prices for Medicare Part B physician-administered drugs. As a result of this legislation and the expansion of federal coverage of pharmaceutical products, there is additional pressure to contain and reduce costs. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors. These cost reduction initiatives and other provisions of the MMA could decrease the coverage and reimbursement that we receive for any approved products, and could seriously harm our business.

In addition, in March 2010, the Affordable Care Act was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, introduced 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, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans, imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs coverage under Medicare Part D, and subjected drug manufacturers to new annual fees based on pharmaceutical companies' share of sales to federal healthcare programs.

On August 2, 2011, the Budget Control Act of 2011 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 included aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013 and will stay in effect through 2024 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals and imaging centers.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products once approved or additional pricing pressures.

**Employees**

As of March 31, 2016, we had 61 full-time employees, 44 of whom were primarily engaged in research and development activities and 26 of whom have an M.D. or Ph.D. degree.

**Facilities**

Our headquarters are located in Cambridge, Massachusetts, where we lease approximately 15,200 square feet of office and laboratory space. Our lease expires in January 2020, and we have an option to extend it through January 2025.

In January 2016, we entered into a ten-year agreement to lease approximately 65,000 square feet of office and laboratory space in Cambridge, which we expect to occupy as our headquarters near the end of 2016. We believe that this new office and laboratory space is sufficient to meet our needs for the foreseeable future and that suitable additional space will be available as and when needed.

**Legal Proceedings**

We are not currently a party to any material legal proceedings.

One United States patent application licensed to us by Caribou is subject to a patent interference proceeding between UC/Vienna and Dr. Emmanuelle Charpentier, on the one hand, and the Broad Institute, MIT and

Harvard on the other hand. See the section entitled “Intellectual Property—Caribou Biosciences In-Licensed Intellectual Property—University of California, Berkeley and University of Vienna IP” appearing elsewhere in this prospectus for more information regarding this patent interference proceeding.

## MANAGEMENT

### Executive Officers and Directors

The following table sets forth the name, age and position of each of our executive officers and directors, as of April 25, 2016:

| Name | Age | Position |
|---|---|---|
| Nessan Bermingham, Ph.D | 43 | Founder, President, Chief Executive Officer and Director |
| Thomas M. Barnes, Ph.D | 56 | Chief Scientific Officer |
| John M. Leonard, M.D | 58 | Chief Medical Officer and Director |
| David V. Morrissey, Ph.D | 58 | Chief Technology Officer |
| José E. Rivera, J.D | 50 | Chief Operating Officer and Chief Legal Officer |
| Sapna Srivastava, Ph.D | 45 | Chief Financial and Strategy Officer |
| Caroline Dorsa(1)(2)(3) | 56 | Director |
| Jean-François Formela, M.D.(1)(2)(3) | 59 | Director |
| Carl L. Gordon, Ph.D.(1)(2) | 51 | Director |
| Rachel Haurwitz, Ph.D | 30 | Director |
| Perry Karsen(2)(3) | 61 | Director, Chairman of the Board of Directors |

(1) Member of the audit committee
(2) Member of the compensation committee
(3) Member of the nominating and corporate governance committee

***Nessan Bermingham, Ph.D.***, has served as our President, Chief Executive Officer and director since he founded the company in May 2014. Prior to founding Intellia, from 2002 to 2007 and 2012 to 2014 Dr. Bermingham held various positions at Atlas Venture, an early stage venture capital firm focused on investments in biological and drug discovery technologies, most recently as venture partner. From 2007 to 2008, he was a partner at Omega Fund Management, a direct secondary healthcare fund, and from 2009 to 2013, he served as the founder and managing partner of Bio Equity Capital LLC, a healthcare focused special situations firm. Dr. Bermingham was the founding Chief Executive Officer of Tal Medical, a clinical stage medical device company, previously worked at UBS AG and sits on the independent advisory board of Merck Serono and on the board of directors of Harbor Antibodies. Dr. Bermingham received his B.S. from Queen's University in Belfast, Northern Ireland, a Ph.D. in molecular biology from Imperial College London and was a Howard Hughes Associate Fellow at Baylor College of Medicine. We believe that Dr. Bermingham's detailed knowledge of our company and his over 15 years in the life sciences industry, provide a valuable contribution to our board of directors.

***Thomas M. Barnes, Ph.D.***, has served as our Chief Scientific Officer since October 2014. Prior to joining Intellia, from 2013 to 2014, Dr. Barnes served as Principal at Barnes Consulting, a consulting company he founded, and from April 2009 to 2013, he was Vice President of Discovery at Eleven Biotherapeutics Inc., a biotechnology company. From 2008 to 2009, Dr. Barnes was the chief executive officer of Tengri Therapeutics, Inc., a biotechnology company. From 2004 to 2008, he held positions of increasing responsibility, including Senior Vice President and site head of the drug repositioning division of Ore Pharmaceuticals, Inc., a biopharmaceutical company. Prior to that Dr. Barnes was at Millennium Pharmaceuticals, a biotechnology company in Cambridge, Massachusetts, which is now a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, where he held positions of increasing responsibility, including Director, Genomic Pharmacology from 1997 to 2004. Dr. Barnes received his B.Sc. in genetics from the University of Sydney in Australia, a Ph.D. in genetics from Cambridge University and completed research fellowships at Harvard Medical School and McGill University.

***John M. Leonard, M.D.***, has served as our Chief Medical Officer since July 2014. Prior to joining Intellia, Dr. Leonard was Chief Scientific Officer and Senior Vice President of Research & Development at AbbVie, Inc., or AbbVie, a biopharmaceutical company, from its spin-out from Abbott Laboratories in January 2013 until retiring at the end of 2013. Prior to the formation of AbbVie, from 2008 to 2012, he was Global Head of Pharmaceutical R&D at Abbott Laboratories, or Abbott, a pharmaceuticals and health care products company. Dr. Leonard has over 30 years of combined experience in medicine, research and management serving in various roles at Abbott beginning in 1992. In addition to the board of directors of Intellia, Dr. Leonard has served on the boards of Quintiles Transnational Holdings Inc., a biopharmaceutical development and commercial outsourcing service, since February 2015, Chimerix, Inc. a biopharmaceutical company, since June 2014 and Vitae Pharmaceuticals, Inc., a biotechnology company, since July 2015. He received a B.A. in biochemistry from the University of Wisconsin at Madison and an M.D. from Johns Hopkins University. Dr. Leonard completed his residency in internal medicine at Stanford University School of Medicine followed by a postdoctoral fellowship in molecular virology at the National Institute of Allergy and Infectious Diseases at the National Institutes of Health. We believe that Dr. Leonard's extensive experience in drug development and the biopharmaceutical industry provides him with the qualifications and skills to serve as a director of our company.

***David V. Morrissey, Ph.D.***, has served as our Chief Technology Officer since July 2014. Prior to joining Intellia, Dr. Morrissey was an executive director at the Novartis Institutes for BioMedical Research, Inc., a biopharmaceutical company, from 2007 to 2014 where he helped establish and head its RNAi therapeutics unit. Prior to Novartis, Dr. Morrissey was the Senior Director of Antiviral Therapeutics at Sirna Therapeutics, Inc. a biotechnology company, from 2005 to 2007. He received his B.S. in biology from Clark University, an M.S. in microbiology from The University of Connecticut, a Ph.D. in biology from Wesleyan University and completed his postdoctoral fellowship at Bristol-Myers Squibb.

***José E. Rivera, J.D.***, has served as our Chief Operating Officer and Chief Legal Officer since April 2015. He joined Intellia in July 2014 as our General Counsel and Chief Talent Officer. Prior to joining Intellia, Mr. Rivera was the Vice President, Chief Ethics and Compliance Officer at AbbVie from its spin-out from Abbott in January 2013 until September 2013. Prior to that, from 1996 to 2012, Mr. Rivera led various legal groups at Abbott as Division Vice President and Associate General Counsel, including the company's intellectual property litigation, legal regulatory and general litigation departments. Mr. Rivera received his B.A. in economics from Boston College and his J.D. from Harvard Law School.

***Sapna Srivastava, Ph.D.***, has served as Chief Financial and Strategy Officer since April 2015. Prior to joining Intellia, from 2012 to 2015, Dr. Srivastava served as an independent strategy advisor to various therapeutic-focused biotechnology companies and co-founded a neuroscience-focused biotechnology company. Prior to that, from 2010 to 2012, she served as a senior analyst and team leader of the biotechnology group at Goldman Sachs, and from 2004 to 2009, she served as a senior biotechnology analyst at Morgan Stanley. She also served as a principal and senior biotechnology analyst at ThinkEquity Partners, LLC from 2003 to 2004. She started her career at J.P. Morgan in 1999. Dr. Srivastava received her B.Sc. from the University of Bombay in India and a Ph.D. in neuroscience from New York University Medical Center.

***Caroline Dorsa*** has served as a member of our board of directors since December 2015. Since 2010, Ms. Dorsa has served as a director with Biogen Inc. Ms. Dorsa served as the Executive Vice President and Chief Financial Officer of Public Service Enterprise Group Incorporated, a diversified energy company, from April 2009 to October 2015 and served on its board of directors from 2003 to April 2009. From February 2008 to April 2009, she served as Senior Vice President, Global Human Health, Strategy and Integration at Merck & Co., Inc., a pharmaceutical company. From November 2007 to January 2008, Ms. Dorsa served as Senior Vice President and Chief Financial Officer of Gilead Sciences, Inc., a life sciences company. From February 2007 to November 2007, she served as Senior Vice President and Chief Financial Officer of Avaya, Inc., a telecommunications company. From 1987 to January 2007, Ms. Dorsa held various financial and operational positions at Merck & Co., Inc., including Vice President and Treasurer, Executive Director of U.S. Customer Marketing and Executive Director of U.S. Pricing and Strategic Planning. Ms. Dorsa received her B.A. in history from Colgate University and her M.B.A. from Columbia University. We believe Ms. Dorsa's operational, financial and accounting expertise and knowledge of the pharmaceutical industry provide her with the qualifications and skills to serve as a director of our company.

***Jean-Francois Formela, M.D.***, has served as a member of our board of directors since our founding in May 2014. Dr. Formela is currently a partner in the life sciences group of Atlas Venture and has served in such capacity since joining Atlas Venture in 1993. Since September 2010, Dr. Formela has served as a director of Egalet Corporation, a publicly-traded biopharmaceutical company, of which he was a co-founder, and where he served as chairman of the board from March 2012 to June 2015. Dr. Formela has served on the boards of RaNA Therapeutics, Inc. and Spero Therapeutics, Inc., since 2011 and 2014, respectively. He was also a founder and previously served as chairman of the board of each these companies. He also serves on the board of directors of the following privately held companies: F-star Biotechnology Limited, Navitor Pharmaceuticals, Inc. and Ataxion Therapeutics, Inc. Within the last five years, Dr. Formela has also served on the boards of directors of the following public companies: Horizon Pharma, Inc., ARCA biopharma, Inc. and Achillion Pharmaceuticals, Inc. Prior to joining Atlas Venture, Dr. Formela served as a senior director of medical marketing and scientific affairs at Schering-Plough Corporation, a pharmaceutical company which merged with Merck & Co., Inc. Dr. Formela began his career as a medical doctor and practiced emergency medicine at Necker University Hospital in Paris. Dr. Formela is a member of the Massachusetts General Hospital Research Advisory Council. He received his M.D. from the Paris University School of Medicine and his M.B.A. from Columbia University. We believe Dr. Formela's experience in the life sciences industry, as well as his practice of medicine, provides him with the qualifications and skills to serve as a director of our company.

***Carl L. Gordon, Ph.D.***, has been a member of our board of directors since August of 2015. Dr. Gordon co-founded OrbiMed Advisors LLC, or OrbiMed, an investment firm focused on the healthcare sector, in 1998 and, since that time, has served as a member and Co-Head of Private Equity. Prior to co-founding OrbiMed, Dr. Gordon was a senior biotechnology analyst at Mehta and Isaly, a pharmaceutical consulting firm and predecessor to OrbiMed, from 1995 to 1997. From 1993 to 1995, Dr. Gordon was a fellow at The Rockefeller University. He received his Ph.D. in Molecular Biology from the Massachusetts Institute of Technology and a bachelor's degree from Harvard College. As a venture capitalist focused on life science companies Dr. Gordon sits on numerous boards, including Adicet Bio, Inc., Adimab, LLC, Alector, LLC, Armo Biosciences, Inc., Arsanis Biosciences, Inc., Compass Therapeutics, Inc., Good Start Genetics, Inc., Igenica, Inc., Oric Pharmaceuticals, Inc., Oxford Development, Selecta Biosciences, Inc., Singulex, Inc., and True North Therapeutics, Inc. In the last five years, he has also served on the boards of Acceleron Pharma, Inc., Acerta Pharma, LLC, ACIR Biosciences, Inc., Amarin Corporation plc, Pacira Pharmaceuticals, Inc. and Seragon Pharmaceuticals, Inc. We believe that Dr. Gordon's financial and operational experience in the biotechnology industry as well as his expertise in molecular biology and financial credentials provide him with the qualifications and skills to serve as a director of our company.

***Rachel Haurwitz, Ph.D.***, has been a member of our board of directors since the company's founding in May 2014. Dr. Haurwitz is the President, Chief Executive Officer and a member of the board of directors of Caribou Biosciences which she co-founded in 2012. Dr. Haurwitz received an A.B. in biological science from Harvard College and a Ph.D. in molecular and cell biology from the University of California, Berkeley. We believe that Dr. Haurwitz's experience in CRISPR/Cas9 development and research provides her with the qualifications and skills to serve as a director of our company.

***Perry Karsen*** has served as the chairman of our board of directors since April 2016. From May 2013 to December 2015, Mr. Karsen served as the Chief Executive Officer of the Celgene Cellular Therapeutics division of Celgene Corporation, a global biopharmaceutical company. Mr. Karsen served as Chief Operations Officer and Executive Vice President of Celgene from July 2010 to May 2013, and as Senior Vice President and Head of Worldwide Business Development of Celgene from 2004 to 2009. Between February 2009 and July 2010, Mr. Karsen was Chief Executive Officer of Pearl Therapeutics, Inc., a privately held biotechnology company that was subsequently acquired by AstraZeneca plc. Prior to his tenure with Celgene, Mr. Karsen held executive positions at Human Genome Sciences, Inc., a biopharmaceutical company subsequently acquired by GlaxoSmithKline, Bristol-Myers Squibb Co., a biopharmaceutical company, Genentech, Inc., a member of the Roche Group, and Abbott. In addition, Mr. Karsen previously served as a general partner at Pequot Ventures, a venture capital firm. He currently serves on the board of directors of Agios Pharmaceuticals, Inc., OncoMed Pharmaceuticals, Inc. and Voyager Therapeutics, Inc. as well as the Gladstone Foundation and the Sonoma Land Trust. He is a past

member of the board of directors of and currently a member of the executive committee of the Biotechnology Innovation Organization and the board of directors of the Alliance for Regenerative Medicine. Mr. Karsen received a masters of management degree from Northwestern University's Kellogg Graduate School of Management, a masters of arts in teaching of biology from Duke University and a B.S. in biological sciences from the University of Illinois, Urbana-Champaign. We believe Mr. Karsen's executive leadership experience, including his experience as an executive at large multi-national pharmaceutical companies and membership on boards of various trade organizations, qualifies him to serve as a member of our board of directors.

**Composition of Our Board of Directors**

Our board of directors currently consists of seven members, each of whom are members pursuant to the board composition provisions of our certificate of incorporation and agreements with our stockholders. These board composition provisions will terminate upon the completion of this offering. Upon the termination of these provisions, there will be no further contractual obligations regarding the election of our directors. Our nominating and corporate governance committee and our board of directors may therefore consider a broad range of factors relating to the qualifications and background of nominees. Our nominating and corporate governance committee's and our board of directors' priority in selecting board members is identification of persons who will further the interests of our stockholders through their established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape, professional and personal experiences and expertise relevant to our growth strategy. Our directors hold office until their successors have been elected and qualified or until the earlier of their resignation or removal. Our amended and restated certificate of incorporation that will become effective upon the closing of this offering and amended and restated bylaws that became effective upon the effectiveness of the registration statement of which this prospectus is a part also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

***Director Independence***

Our board of directors has determined that all members of the board of directors, except Drs. Bermingham, Leonard and Haurwitz, are independent directors, including for purposes of the rules of The NASDAQ Global Market and the Securities and Exchange Commission, or SEC. In making such independence determination, our board of directors considered the relationships that each non-employee director has with us and all other facts and circumstances that our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director. In considering the independence of the directors listed above, our board of directors considered the association of our directors with the holders of more than 5% of our common stock. Upon the completion of this offering, we expect that the composition and functioning of our board of directors and each of our committees will comply with all applicable requirements of The NASDAQ Global Market and the rules and regulations of the SEC. There are no family relationships among any of our directors or executive officers. Drs. Bermingham and Leonard are not independent directors under these rules because they are executive officers of the Company and Dr. Haurwitz is not an independent director under these rules because of her affiliation with Caribou.

***Staggered Board***

In accordance with the terms of our amended and restated certificate of incorporation that will become effective upon the closing of this offering and amended and restated bylaws that became effective upon the effectiveness of the registration statement of which this prospectus is a part, our board of directors will be divided into three staggered classes of directors and each will be assigned to one of the three classes. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the

directors of the same class whose terms are then expiring. The terms of the directors will expire upon the election and qualification of successor directors at the annual meeting of stockholders to be held during the years 2017 for Class I directors, 2018 for Class II directors and 2019 for Class III directors.

- Our Class I directors will be Drs. Bermingham and Formela;
- Our Class II directors will be Drs. Gordon and Haurwitz; and
- Our Class III directors will be Ms. Dorsa, Mr. Karsen and Dr. Leonard.

Our amended and restated certificate of incorporation that will become effective upon the closing of this offering and amended and restated by-laws that became effective upon the effectiveness of the registration statement of which this prospectus is a part provide that the number of our directors shall be fixed from time to time by a resolution of the majority of our board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

**Board Leadership Structure and Board's Role in Risk Oversight**

Currently, the role of chairman of the board is separated from the role of Chief Executive Officer, and we plan to keep these roles separated following the completion of this offering. We believe that separating these positions allows our Chief Executive Officer to focus on our day-to-day business, while allowing a chairman of the board to lead the board of directors in its fundamental role of providing advice to and independent oversight of management. Our board of directors recognizes the time, effort and energy that the Chief Executive Officer is required to devote to his position in the current business environment, as well as the commitment required to serve as our chairman, particularly as the board of directors' oversight responsibilities continue to grow. While our amended and restated by-laws and corporate governance guidelines do not require that our chairman and Chief Executive Officer positions be separate, our board of directors believes that having separate positions is the appropriate leadership structure for us at this time and demonstrates our commitment to good corporate governance.

Risk is inherent with every business, and how well a business manages risk can ultimately determine its success. We face a number of risks, including risks relating to our financial condition, development and commercialization activities, operations, strategic direction and intellectual property as more fully discussed in the section entitled "Risk Factors" appearing elsewhere in this prospectus. Management is responsible for the day-to-day management of risks we face, while our board of directors, as a whole and through its committees, has responsibility for the oversight of risk management. In its risk oversight role, our board of directors has the responsibility to satisfy itself that the risk management processes designed and implemented by management are adequate and functioning as designed.

The role of the board of directors in overseeing the management of our risks is conducted primarily through committees of the board of directors, as disclosed in the descriptions of each of the committees below and in the charters of each of the committees. The full board of directors (or the appropriate board committee in the case of risks that are under the purview of a particular committee) discusses with management our major risk exposures, their potential impact on us, and the steps we take to manage them. When a board committee is responsible for evaluating and overseeing the management of a particular risk or risks, the chairman of the relevant committee reports on the discussion to the full board of directors during the committee reports portion of the next board meeting. This enables the board of directors and its committees to coordinate the risk oversight role, particularly with respect to risk interrelationships.

**Committees of Our Board of Directors**

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which will operate pursuant to a charter adopted by our board of directors that became effective upon the effectiveness of the registration statement of which this prospectus is a

part. The composition and functioning of all of our committees currently comply with all applicable requirements of the Sarbanes-Oxley Act of 2002, NASDAQ and SEC rules and regulations.

***Audit Committee***

Ms. Dorsa, Dr. Formela and Dr. Gordon serve on the audit committee, which is chaired by Ms. Dorsa. Our board of directors has determined that Ms. Dorsa, Dr. Formela and Dr. Gordon are "independent" for audit committee purposes as that term is defined in the rules of the SEC and the applicable NASDAQ rules, and each has sufficient knowledge in financial and auditing matters to serve on the audit committee. Our board of directors has designated Ms. Dorsa as an "audit committee financial expert," as defined under the applicable rules of the SEC. The audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending based upon the audit committee's review and discussions with management and our independent registered public accounting firm whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related person transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing quarterly earnings releases.

***Compensation Committee***

Ms. Dorsa, Dr. Formela, Dr. Gordon and Mr. Karsen serve on the compensation committee, which is chaired by Dr. Formela. Our board of directors has determined that each member of the compensation committee is "independent" as defined in the applicable NASDAQ rules. The compensation committee's responsibilities include:

- annually reviewing and recommending to the board of directors the corporate goals and objectives relevant to the compensation of our Chief Executive Officer;
- evaluating the performance of our Chief Executive Officer in light of such corporate goals and objectives and based on such evaluation: (i) recommending to the board of directors the cash compensation of our Chief Executive Officer and (ii) reviewing and approving grants and awards to our Chief Executive Officer under equity-based plans;

- reviewing and recommending to the board of directors the cash compensation of our executive officers other than our Chief Executive Officer;
- determining the equity compensation of our executive officers other than our Chief Executive Officer under equity-based plans;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;
- evaluating and assessing potential and current compensation advisors in accordance with the independence standards identified in the applicable NASDAQ rules;
- retaining and approving the compensation of any compensation advisors;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- reviewing and recommending to the board of directors the compensation of our directors;
- preparing the compensation committee report required by SEC rules, if and when required, to be included in our annual proxy statement; and
- reviewing and approving the retention or termination of any consulting firm or outside advisor to assist in the evaluation of compensation matters.

***Nominating and Corporate Governance Committee***

Ms. Dorsa, Dr. Formela and Mr. Karsen serve on the nominating and corporate governance committee, which is chaired by Mr. Karsen. Our board of directors has determined that each member of the nominating and corporate governance committee is "independent" as defined in the applicable NASDAQ rules. The nominating and corporate governance committee's responsibilities include:

- developing and recommending to the board of directors criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;
- reviewing the composition of the board of directors to ensure that it is composed of members containing the appropriate skills and expertise to advise us;
- identifying individuals qualified to become members of the board of directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board's committees;
- developing and recommending to the board of directors a code of business conduct and ethics and a set of corporate governance guidelines; and
- overseeing the evaluation of our board of directors and management.

Our board of directors may from time to time establish other committees.

**Compensation Committee Interlocks and Insider Participation**

None of the members of our compensation committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

**Corporate Governance**

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the code has been posted on the Corporate

Governance section of our website, which is located at www.intelliatx.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

## EXECUTIVE COMPENSATION

### Executive Compensation Overview

Our executive compensation program has reflected our growth and development-oriented corporate culture. To date, the compensation of our Chief Executive Officer and our other executive officers identified in the Summary Compensation Table below, who we refer to as the named executive officers, has primarily consisted of a combination of base salary, bonuses and long-term incentive compensation in the form of restricted stock awards. Our named executive officers, like all full-time employees, are eligible to participate in our health and welfare benefit plans. As we transition from a private company to a publicly traded company, we will evaluate our compensation values and philosophy and compensation plans and arrangements as circumstances require. At a minimum, we expect to review executive compensation annually with input from a compensation consultant. As part of this review process, we expect the board of directors and the compensation committee to apply our values and philosophy, while considering the compensation levels needed to ensure our executive compensation program remains competitive. We will also review whether we are meeting our retention objectives and the potential cost of replacing a key employee.

### Summary Compensation Table

The following table presents information regarding the total compensation awarded to, earned by, and paid to our named executive officers for services rendered to us in all capacities for the years indicated.

| Name and Principal Position | | Salary ($) | Bonus ($)(1) | Stock Awards ($)(2) | All Other Compensation ($)(3) | Total ($) |
|---|---|---|---|---|---|---|
| Nessan Bermingham, Ph.D.(4) | 2015 | 383,333 | 180,000 | — | — | 563,333 |
| *Founder, President and Chief Executive Officer* | 2014 | 151,668 | 175,000 | 320,368 | — | 647,036 |
| Sapna Srivastava, Ph.D.(5) | 2015 | 220,000 | 73,200 | 221,689 | 25,630 | 540,519 |
| *Chief Financial and Strategy Officer* | | | | | | |
| José E. Rivera, J.D.(6) | 2015 | 325,000 | 123,750 | — | 47,445 | 496,195 |
| *Chief Operating Officer and Chief Legal Officer* | 2014 | 150,000 | 81,250 | 52,719 | 11,006 | 294,975 |

(1) The amounts reflect the discretionary bonus paid in the subsequent year for performance during the year indicated.

(2) Amounts reflect the grant date fair value of equity-based awards granted in the year in accordance with Financial Accounting Standards Board, Accounting Standards Codification Topic 718, or ASC 718. Such grant-date fair value does not take into account any estimated forfeitures related to service-vesting conditions. These amounts do not correspond to the actual value that may be recognized by the named executive officers upon vesting of the applicable awards.

(3) Amounts exclude medical, group life insurance and certain other benefits received by the named executive officers that are available generally to all of our salaried employees on the same terms. The amounts reported represent travel and lodging expenses related to travel between the applicable named executive officer's home office and our headquarters in Massachusetts. For 2015, such amounts include (i) transportation expenses of $16,322 for Dr. Srivastava and $21,414 for Mr. Rivera, (ii) lodging expenses of $9,234 for Dr. Srivastava and $25,180 for Mr. Rivera and (iii) meals expense of $74 for Dr. Srivastava and $851 for Mr. Rivera.

(4) Dr. Bermingham commenced employment with us on December 1, 2014. His annualized base salary for 2014 was $350,000. The amount reported for 2014 also includes amounts paid to Dr. Bermingham pursuant to a consulting agreement with us, dated July 31, 2014, pursuant to which he was paid $29,167 per month from July 2014 through November 2014 for consulting services provided to us.

(5) Dr. Srivastava commenced employment with us on April 6, 2015. Her annualized base salary for 2015 was $300,000.

(6) Mr. Rivera commenced employment with us on October 1, 2014. His annualized base salary for 2014 was $300,000. The amount reported for 2014 also includes amounts paid to Mr. Rivera pursuant to a consulting agreement with us, dated July 31, 2014, pursuant to which he was paid $25,000 per month from July 2014 through November 2014 for consulting services provided to us.

***Employment Arrangements with our Named Executive Officers***

We have an offer letter agreement with each of our named executive officers in connection with their employment with us. These offer letters provide for "at will" employment.

***Nessan Bermingham, Ph.D.*** On December 15, 2014, we entered into a letter agreement with Dr. Bermingham for the position of Chief Executive Officer and President. Dr. Bermingham currently receives an annual base salary of $450,000, which is subject to review and adjustment in accordance with company policy. Dr. Bermingham is also eligible for an annual discretionary bonus of up to 40% of his base salary, payable at the discretion of the board of directors. Dr. Bermingham is eligible to participate in employee benefit plans generally available to our executive employees, subject to the terms of those plans.

***Sapna Srivastava, Ph.D.*** On April 6, 2015, we entered into a letter agreement with Dr. Srivastava for the position of Chief Financial and Strategy Officer. Dr. Srivastava currently receives an annual base salary of $300,000, which is subject to review and adjustment in accordance with company policy. Dr. Srivastava is also eligible for an annual discretionary bonus of up to 33% of her base salary, payable at the discretion of the board of directors. Dr. Srivastava is eligible to participate in employee benefit plans generally available to our executive employees, subject to the terms of those plans.

***José E. Rivera, J.D.*** On September 30, 2014, we entered into a letter agreement with Mr. Rivera for the position of General Counsel and Chief Talent Officer. Mr. Rivera currently receives an annual base salary of $375,000, which is subject to review and adjustment in accordance with company policy. Mr. Rivera is also eligible for an annual discretionary bonus of up to 33% of his base salary, payable at the discretion of the board of directors. Mr. Rivera is eligible to participate in employee benefit plans generally available to our executive employees, subject to the terms of those plans.

Our board of directors has approved employment agreements for each of our named executive officers, which will become effective upon the closing of this offering. These employment agreements provide for "at will" employment and will supersede and replace in all respects the terms of the offer letter agreements for our named executive officers described above.

Under the employment agreements, each of our named executive officers will be entitled to receive the same base salary and be eligible to receive a performance bonus with the same target percentage of base salary, in each case as set forth in such officer's current offer letter agreement. Each named executive officer will also be eligible to participate in the employee benefit plans generally available to full-time employees, subject to the terms of those plans. If a named executive officer's employment is terminated by us without cause, as defined in the officer's employment agreement, or by the named executive officer for good reason, as defined in the officer's employment agreement, and subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, the named executive officer will be entitled to receive: (i) an amount equal to 12 months of base salary in the case of Dr. Bermingham and nine months of base salary in the case of Dr. Srivastava and Mr. Rivera, in each case, payable in substantially equal installments over nine or 12 months, as applicable, following the officer's termination, and (ii) if the named executive officer is participating in our group health plan immediately prior to his or her termination, a monthly cash payment until the earlier of 12 months in the case of Dr. Bermingham or nine months in the case of Dr. Srivastava and Mr. Rivera, in each case, following termination or the end of the officer's COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to the officer had he or she remained employed with us. In addition, all time-based equity awards held by the named executive officer or by entities to which the named executive officer has properly transferred such awards that would have vested in the applicable nine or 12-month period following the officer's termination had he or she remained employed by us during such period will accelerate and vest as of the date of termination. In lieu of the payments and benefits described above, in the event that the named executive officer's employment is terminated by us without cause or the named executive officer resigns for "good reason," as defined in the officer's employment agreement, in either case within 12 months following a "change in control," as defined in the officer's employment agreement, subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, the

named executive officer will be entitled to receive (i) in the case of Dr. Bermingham, a lump sum cash payment equal to 18 months of his then-current base salary, or his base salary in effect immediately prior to the change in control, if higher, or, in the case of Dr. Srivastava and Mr. Rivera, 12 months of the officer's then-current base salary, or the officer's base salary in effect immediately prior to the change in control, if higher, in each case, plus the officer's target bonus, (ii) if the officer is participating in our group health plan immediately prior to his or her termination, a monthly cash payment until the earlier of 12 or 18 months, as applicable, following termination or the end of the officer's COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to him had he or she remained employed with us and (iii) full acceleration of all time-based equity awards held by the officer or by entities to whom the officer has properly transferred such awards.

***Employee Confidentiality, Non-Competition, Non-Solicitation and Assignment Agreements***

Each of our named executive officers has entered into a standard form agreement with respect to confidential information and assignment of inventions. Among other things, this agreement obligates each named executive officer to refrain from disclosing any of our proprietary information received during the course of employment and to assign to us any inventions conceived or developed during the course of employment. Such agreement also provides that during the period of the named executive officer's employment and for six months thereafter, the named executive officer will not compete with us and will not solicit our employees, consultants, customers or suppliers.

**Outstanding Equity Awards at 2015 Fiscal Year-End**

The following table sets forth information concerning outstanding equity awards held by each of our named executive officers as of December 31, 2015. All equity awards in the table below were issued upon conversion of awards made by Intellia Therapeutics, LLC prior to the Reorganization.

| | Stock Awards | |
|---|---|---|
| Name | Number of Shares That Have Not Vested (#) | Market Value of Shares of Stock That Have Not Yet Vested ($)(1) |
| Nessan Bermingham, Ph.D | 225,793(2) | 4,064,274 |
| Sapna Srivastava, Ph.D | 159,031(3) | 2,862,558 |
| José E. Rivera, J.D | 169,344(4) | 3,048,192 |

(1) There was no public market for our common stock on December 31, 2015. We have estimated the market value of the unvested stock award based on an initial public offering price of $18.00 per share.

(2) Represents a restricted stock award for 349,614 shares of our common stock. This restricted stock award vests as follows: 25% of the shares vested and became nonforfeitable on July 31, 2015, and the remainder of the shares vest and become nonforfeitable in substantially equal monthly installments over the following 36 months, subject to Dr. Bermingham's continued service to us.

(3) This restricted stock award vests as follows: 25% of the shares will vest and become nonforfeitable on April 6, 2016 and the remainder of the shares vest and become nonforfeitable in substantially equal monthly installments over the following 36 months, subject to Dr. Srivastava's continued service to us.

(4) Represents a restricted stock award for 262,210 shares of our common stock. This restricted stock award vests as follows: 25% of the shares vested and became nonforfeitable on July 31, 2015, and the remainder of the shares vest and become nonforfeitable in substantially equal monthly installments over the following 36 months, subject to Mr. Rivera's continued service to us. This restricted stock award is held by Rivak Capital LLC. Mr. Rivera is a member and manager of Rivak Capital LLC.

**Compensation Risk Assessment**

We believe that although a portion of the compensation provided to our executive officers and other employees is performance-based, our executive compensation program does not encourage excessive or unnecessary risk taking. This is primarily due to the fact that our compensation programs are designed to

encourage our executive officers and other employees to remain focused on both short-term and long-term strategic goals. As a result, we do not believe that our compensation programs are reasonably likely to have a material adverse effect on us.

**Employee Benefit and Equity Compensation Plans**

***2015 Stock Plan***

Our 2015 Plan was approved by our board of directors and stockholders in August 2015 and was most recently amended in February 2016 to increase the number of shares reserved for issuance. We reserved an aggregate of 5,673,226 shares of our common stock for the issuance of awards under the 2015 Plan. This number is subject to adjustment in the event of a subdivision of outstanding stock, a stock dividend, a combination or consolidation of stock, a reclassification, or any other increase or decrease in the number of issued shares of common stock. Effective upon the closing of this offering, our 2015 Plan will be restated as our 2015 Restated Plan. The shares of common stock underlying any awards that are canceled or reacquired by us or are withheld by us for payment of the purchase price, exercise price or withholding taxes under the 2015 Plan are added back to the shares of common stock available for issuance under the 2015 Plan. Upon the closing of this offering, such shares will be added to the shares of common stock available for issuance under the 2015 Restated Plan.

The 2015 Plan is administered by our board of directors. The administrator has full authority and discretion to take any actions it deems necessary or advisable for the administration of the 2015 Plan.

Our employees, outside directors and consultants are eligible to receive awards under the 2015 Plan.

The 2015 Plan provides that upon the effectiveness of a "sale event," as defined in the 2015 Plan, an acquirer or successor entity may assume, continue or substitute outstanding awards under the 2015 Plan. To the extent that awards granted under the 2015 Plan are not assumed or continued or substituted by the successor entity, upon the effective time of the sale event, the 2015 Plan and all outstanding awards thereunder shall terminate. In the event of such termination, except to the extent otherwise provided in the relevant award certificate, all options and stock appreciation rights that are not exercisable immediately prior to the effective time of the sale event shall become fully exercisable as of the effective time of the sale event, all other awards with time based vesting, conditions or restrictions, shall become fully vested and nonforfeitable as of the effective time of the sale event and all awards with conditions and restrictions relating to the attainment of performance goals may become vested and nonforfeitable in the discretion of the administrator or to the extent specified in the relevant award certificate. In addition, in connection with the termination of the 2015 Plan upon a sale event, we may make or provide for a cash payment to participants holding vested and exercisable options and stock appreciation rights equal to the difference between the per share cash consideration payable to stockholders in the sale event and the exercise price of the options or stock appreciation rights or each grantee shall be permitted within a specified period of time prior to the sale event, to exercise all outstanding stock options and stock appreciation rights held by such grantee to the extent exercisable.

Our board of directors may amend or discontinue the 2015 Plan and the administrator may amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose, but no such action may adversely affect rights under an award without the holder's consent. Certain amendments to the 2015 Plan require the approval of our stockholders.

***Amended and Restated 2015 Stock Option and Incentive Plan***

Our 2015 Restated Plan was adopted by our board of directors on January 19, 2016, approved by our stockholders on April 22, 2016 and amended on April 26, 2016. The 2015 Restated Plan became effective on the date immediately prior to the date on which the registration statement of which this prospectus is part was declared effective by the SEC. The 2015 Restated Plan amended and restated the 2015 Plan. The 2015 Restated Plan allows the board of directors and the compensation committee to make equity-based incentive awards to our officers, employees, directors and other key persons (including consultants).

We have initially reserved 7,058,823 shares of our common stock for the issuance of awards under the 2015 Restated Plan, or the Initial Limit. The 2015 Restated Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2017, by 4% of the outstanding number of shares of our common stock on the immediately preceding December 31 or such lesser number of shares as determined by our compensation committee, or the Annual Increase. The Initial Limits and other share limited in the 2015 Restated Plan are subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

The shares we issue under the 2015 Restated Plan will be authorized but unissued shares or shares that we acquire. The shares of common stock underlying any awards that are forfeited, cancelled, held back upon exercise of an option or settlement of an award to cover the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without the issuance of stock or are otherwise terminated (other than by exercise) under the 2015 Restated Plan will be added back to the shares of common stock available for issuance under the 2015 Restated Plan.

Stock options and stock appreciation rights with respect to no more than the Initial Limit may be granted to any one individual in any one calendar year. The maximum number of shares that may be issued as incentive stock options may not exceed the Initial Limit cumulatively increased on January 1, 2017 and on each January 1 thereafter by the lesser of the Annual Increase or 7,058,823 shares. The value of all awards made under the 2015 Restated Plan and all other cash compensation paid by us to any non-employee director in any calendar year shall not exceed $1.0 million.

The 2015 Restated Plan will be administered by our compensation committee. Our compensation committee has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, to make any combination of awards to participants, and to determine the specific terms and conditions of each award, subject to the provisions of the 2015 Restated Plan. Persons eligible to participate in the 2015 Restated Plan will be those full or part-time officers, employees, non-employee directors and consultants as selected from time to time by our compensation committee in its discretion.

The 2015 Restated Plan permits the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code and options that do not so qualify. The option exercise price of each option will be determined by our compensation committee but may not be less than 100% of the fair market value of our common stock on the date of grant. The term of each option will be fixed by our compensation committee and may not exceed ten years from the date of grant. Our compensation committee will determine at what time or times each option may be exercised.

Our compensation committee may award stock appreciation rights subject to such conditions and restrictions as it may determine. Stock appreciation rights entitle the recipient to shares of common stock, or cash, equal to the value of the appreciation in our stock price over the exercise price. The exercise price may not be less than 100% of the fair market value of our common stock on the date of grant. The term of each stock appreciation right will be fixed by our compensation committee and may not exceed ten years from the date of grant. Our compensation committee will determine at what time or times each stock appreciation right may be exercised.

Our compensation committee may award restricted shares of common stock and restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and/or continued employment with us through a specified vesting period. Our compensation committee may also grant shares of common stock that are free from any restrictions under the 2015 Restated Plan. Unrestricted stock may be granted to participants in recognition of past services or for other valid consideration and may be issued in lieu of cash compensation due to such participant.

Our compensation committee may grant performance share awards to participants that entitle the recipient to receive awards of common stock upon the achievement of certain performance goals and such other conditions as our compensation committee may determine. Our compensation committee may grant dividend equivalent rights to participants that entitle the recipient to receive credits for dividends that would be paid if the recipient had held a specified number of shares of common stock.

Our compensation committee may grant cash bonuses under the 2015 Restated Plan to participants, subject to the achievement of certain performance goals.

Our compensation committee may grant awards of restricted stock, restricted stock units, performance share awards or cash-based awards under the 2015 Restated Plan that are intended to qualify as "performance-based compensation" under Section 162(m) of the Code. Such awards will only vest or become payable upon the attainment of performance goals that are established by our compensation committee and related to one or more performance criteria. The performance criteria that could be used with respect to any such awards are limited to: total stockholder return, earnings before interest, taxes, depreciation and amortization, net income (loss) (either before or after interest, taxes, depreciation and/or amortization), changes in the market price of our common stock, economic value-added, funds from operations or similar measure, sales or revenue, development, clinical, regulatory or commercial milestones, acquisitions or strategic transactions, including licenses, collaborations, joint ventures or promotional arrangements, operating income (loss), cash flow (including, but not limited to, operating cash flow and free cash flow), return on capital, assets, equity, or investment, return on sales, gross or net profit levels, productivity, expense, margins, operating efficiency, customer satisfaction, working capital, earnings (loss) per share of our common stock, sales or market shares and number of customers, any of which may be measured either in absolute terms or as compared to any incremental increase or as compared to results of a peer group. From and after the time that we become subject to Section 162(m) of the Code, the maximum award that is intended to qualify as "performance-based compensation" under Section 162(m) of the Code that may be made to certain of our officers during any one calendar year period is 2,500,000 shares of common stock with respect to a share-based award and $5.0 million with respect to a cash-based award.

The 2015 Restated Plan provides that upon the effectiveness of a "sale event," as defined in the 2015 Restated Plan, an acquirer or successor entity may assume, continue or substitute outstanding awards under the 2015 Restated Plan. In the event that awards are assumed, continued or substituted in connection with a sale event and a grantee's employment or other service relationship is terminated without cause by the Company, or its successor, or a grantee's employment is terminated by the grantee for good reason, in either case in connection with or within 12 months following the sale event, (i) except as may otherwise be provided in the relevant award certificate, all awards held by such grantee with time-based vesting, conditions or restrictions shall become fully vested and nonforfeitable as of the effective time of such termination, and (ii) all awards held by such grantee with conditions and restrictions relating to the attainment of performance goals may become vested and nonforfeitable in the discretion of the administrator or the extent specified in the relevant award certificate. To the extent that awards granted under the 2015 Restated Plan are not assumed or continued or substituted by the successor entity, upon the effective time of the sale event, the 2015 Restated Plan and all awards thereunder shall terminate. In the event of such termination, except as may otherwise be provided in the relevant award certificate, all options and stock appreciation rights that are not exercisable immediately prior to the effective time of the sale event shall become fully exercisable as of the effective time of the sale event, all other awards with time based vesting, conditions or restrictions, shall become fully vested and nonforfeitable as of the effective time of the sale event and all awards with conditions and restrictions relating to the attainment of performance goals may become vested and nonforfeitable in the discretion of the administrator or to the extent specified in the relevant award certificate. In addition, in connection with the termination of the 2015 Restated Plan and awards thereunder upon a sale event, we may make or provide for a cash payment to participants holding vested and exercisable options and stock appreciation rights equal to the difference between the per share cash consideration payable to stockholders in the sale event and the exercise price of the options or stock appreciation rights or each grantee, shall be permitted within a specified period of time prior to the sale event, to exercise all outstanding stock options and stock appreciation rights held by such grantee to the extent exercisable. We shall also have the option to make or provide for payment, in cash or in kind, to the grantees of other awards equal to the per share cash consideration payable to stockholders in the sale event multiplied by the number of vested shares of common stock subject to such awards.

Our board of directors may amend or discontinue the 2015 Restated Plan and our compensation committee may amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose, but no such action may adversely affect rights under an award without the holder's consent. Certain amendments to the 2015 Restated Plan require the approval of our stockholders.

No awards may be granted under the 2015 Restated Plan after the date that is ten years from the date of stockholder approval of the 2015 Restated Plan. Our board of directors has approved the issuance under the 2015 Restated Plan of incentive and non-qualified stock options to acquire an aggregate of 308,592 shares of common stock on the effective date of the registration statement of which this prospectus is a part. These stock options will have an exercise price equal to the public offering price. No other awards under the 2015 Restated Plan have been made prior to the date hereof.

***2016 Employee Stock Purchase Plan***

Our 2016 Employee Stock Purchase Plan, or ESPP, was adopted by our board of directors on January 19, 2016 and approved by our stockholders on April 22, 2016 and became effective on the date immediately prior to the date on which the registration statement of which this prospectus is part was declared effective by the SEC. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423(b) of the Code. The ESPP initially reserves and authorizes the issuance of up to a total of 441,176 shares of common stock to participating employees. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2017 and each January 1 thereafter through January 1, 2026, by the least of (i) 1% of the outstanding number of shares of our common stock on the immediately preceding December 31; (ii) 500,000 shares or (iii) such number of shares as determined by the ESPP administrator. The number of shares reserved under the ESPP is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

All employees who have completed at least 30 days of employment and whose customary employment is for more than 20 hours per week are eligible to participate in the ESPP. However, any employee who owns 5% or more of the total combined voting power or value of all classes of stock is not eligible to purchase shares under the ESPP.

We will make one or more offerings each year to our employees to purchase shares under the ESPP. Offerings will usually begin on each January 1 and July 1 and will continue for six-month periods, referred to as offering periods. Each eligible employee may elect to participate in any offering by submitting an enrollment form at least 15 business days before the relevant offering date.

Each employee who is a participant in the ESPP may purchase shares by authorizing payroll deductions of up to 10% of his or her base compensation during an offering period. Unless the participating employee has previously withdrawn from the offering, his or her accumulated payroll deductions will be used to purchase shares on the last business day of the offering period at a price equal to 85% of the fair market value of the shares on the first business day or the last business day of the offering period, whichever is lower. Under applicable tax rules, an employee may purchase no more than $25,000 worth of shares of common stock, valued at the start of the purchase period, under the ESPP in any calendar year.

The accumulated payroll deductions of any employee who is not a participant on the last day of an offering period will be refunded. An employee's rights under the ESPP terminate upon voluntary withdrawal from the plan or when the employee ceases employment with us for any reason.

The ESPP may be terminated or amended by our board of directors at any time. An amendment that increases the number of shares of common stock authorized under the ESPP and certain other amendments require the approval of our stockholders.

***Senior Executive Cash Incentive Bonus Plan***

Our Senior Executive Cash Incentive Bonus Plan, or the Bonus Plan, was adopted by our board of directors on January 19, 2016. The Bonus Plan provides for cash bonus payments based upon the attainment of performance targets established by our compensation committee. The payment targets will be related to financial and operational measures or objectives with respect to our company, or Corporate Performance Goals, as well as individual performance objectives.

Our compensation committee may select Corporate Performance Goals from among the following: cash flow (including, but not limited to, operating cash flow and free cash flow); revenue; corporate revenue; earnings before interest, taxes, depreciation and amortization; net income (loss) (either before or after interest, taxes, depreciation and/or amortization); changes in the market price of our common stock; economic value-added; funds from operations or similar measure, sales or revenue, developmental, clinical or regulatory milestones, acquisitions or strategic transactions, including licenses, collaborations, joint ventures or promotion arrangements; operating income (loss); return on capital, assets, equity, or investment; total stockholder returns; return on sales; gross or net profit levels; productivity; expense efficiency; margins; operating efficiency; customer satisfaction; working capital; earnings (loss) per share stock; sales or market shares; number of customers, number of new customers or customer references; operating income and/or net annual recurring revenue, any of which may be measured in absolute terms or compared to any incremental increase, in terms of growth, compared to another company or companies or to results of a peer group, against the market as a whole and/or as compared to applicable market indices and/or measured on a pre-tax or post-tax basis (if applicable).

Each executive officer who is selected to participate in the Bonus Plan will have a target bonus opportunity set for each performance period. The bonus formulas will be adopted in each performance period by the compensation committee and communicated to each executive. The Corporate Performance Goals will be measured at the end of each performance period after our financial reports have been published or such other appropriate time as the compensation committee determines. If the Corporate Performance Goals and individual performance objectives are met, payments will be made as soon as practicable following the end of each performance period. The Bonus Plan also permits the compensation committee to approve additional bonuses to executive officers in its sole discretion.

***401(k) Plan***

We maintain a tax-qualified retirement plan that provides eligible employees with an opportunity to save for retirement on a tax-advantaged basis. All participants' interests in their contributions are 100% vested when contributed. Pre-tax contributions are allocated to each participant's individual account and are then invested in selected investment alternatives according to the participants' directions. The retirement plan is intended to qualify under Section 401(a) of the Code. We do not currently make discretionary contributions or matching contributions to our 401(k) plan.

## DIRECTOR COMPENSATION

The following table presents the total compensation for each person who served as a non-employee member of our board of directors during the year ended December 31, 2015. Other than as set forth in the table and described more fully below, we did not pay any compensation, make any equity awards or non-equity awards to or pay any other compensation to any of the non-employee members of our board of directors in 2015. We reimburse non-employee members of our board of directors for reasonable travel expenses. Dr. Nessan Bermingham, our Founder, President and Chief Executive Officer, Dr. John M. Leonard, our Chief Medical Officer, Dr. Jean-François Formela, Dr. Carl Gordon, Dr. Rachel Haurwitz and Dr. Andrew May did not receive any compensation for their respective service as members of our board of directors during fiscal year 2015. Dr. Bermingham's compensation for service as an employee is presented in the "Summary Compensation Table."

| Name | Fees Earned or Paid in Cash ($) | Equity Awards ($)(1) | Total ($) |
|---|---|---|---|
| Caroline Dorsa | $ 2,877 | $ 77,544 | $80,421 |

(1) Amount reflects the grant date fair value of an option award granted in 2015 in accordance with ASC 718. Such grant-date fair value does not take into account any estimated forfeitures related to service-vesting conditions. These amounts do not correspond to the actual value that may be recognized by the named director upon vesting of the applicable awards. As of December 31, 2015, Ms. Dorsa held an option to purchase 16,588 shares of our common stock, which vests over a three-year period.

### Non-Employee Director Compensation Policy

Our board of directors has adopted a non-employee director compensation policy, effective as of the completion of this offering, that is designed to enable us to attract and retain, on a long-term basis, highly qualified non-employee directors. Under the policy, each director who is not an employee will be paid cash compensation from and after the completion of this offering, as set forth below:

| | Member Annual Fee | Chairman Additional Annual Fee |
|---|---|---|
| Board of Directors | $35,000 | $ 25,000 |
| Audit Committee | 7,500 | 7,500 |
| Compensation Committee | 5,000 | 5,000 |
| Nominating and Corporate Governance Committee | 3,500 | 3,500 |

In addition, each non-employee director serving on our board of directors was granted non-qualified stock options on the date of the effectiveness of the registration statement of which this prospectus is a part, as set forth below:

| Name | Non-qualified Stock Options (#) |
|---|---|
| Caroline Dorsa | 15,176 |
| Jean-François Formela, M.D | 23,529 |
| Carl L. Gordon, Ph.D., CFA | 23,529 |
| Rachel E. Haurwitz, Ph.D. | 23,529 |
| Perry Karsen | 31,764 |

Each non-employee director elected or appointed to our board of directors following the completion of this offering will be granted a non-qualified stock option to purchase 31,764 shares of common stock on the date of such director's election or appointment to the board of directors. These stock options will vest as to 33 1/3 % of the total award one year after the date of grant and thereafter in substantially equal quarterly installments during the three years following the grant date, subject to continued service through such date. On the date of each annual meeting of stockholders of our company, each non-employee director will be granted a non-qualified stock option to purchase 10,500 shares of common stock, which will vest and become fully exercisable upon the earlier to occur of the first anniversary of the grant date or the date of the next annual meeting of stockholders following the date of grant, subject to continued service as a director through such date.

## CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Other than the compensation agreements and other arrangements described under "Executive and Director Compensation" in this prospectus and the transactions described below, since our inception on May 7, 2014, there has not been and there is not currently proposed, any transaction or series of similar transactions to which we were, or will be, a party in which the amount involved exceeded, or will exceed, $120,000 and in which any director, executive officer, holder of five percent or more of any class of our capital stock or any member of the immediate family of, or entities affiliated with, any of the foregoing persons, had, or will have, a direct or indirect material interest.

**License Agreement and Services Agreement with Caribou Biosciences, Inc.**

In July 2014 we entered into a license agreement with Caribou Biosciences, Inc., or Caribou. We also entered into a related services agreement with Caribou in July 2014. See the section entitled "Business—Intellectual Property—Caribou Biosciences In-Licensed Intellectual Property" appearing elsewhere in this prospectus for more information. Rachel Haurwitz, a member of our board of directors, and Andrew May, a former member of our board of directors, are executive officers and stockholders of Caribou. Dr. Haurwitz is the President and Chief Executive Officer and a member of the board of Caribou. Dr. May currently serves as the Chief Scientific Officer of Caribou. Caribou Therapeutics Holdco, LLC, a holding company owned and managed by Caribou, is a greater than 5% stockholder in our company. Pursuant to the terms of the license agreement with Caribou, we hold an exclusive, worldwide license, or the Caribou license, for the use of any CRISPR/Cas9-related patents and applications that Caribou had developed and filed, as well as any CRISPR/Cas9-related intellectual property developed by Caribou between July 16, 2014 and the time period specified in the license agreement 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. Pursuant to the services agreement entered into with Caribou in parallel with the license agreement, we are also receiving research and development services from Caribou until November 2016.

In relation to our founding, on July 16, 2014, Intellia Therapeutics, LLC, our former sole stockholder and holding company parent, issued junior preferred units to Caribou Therapeutics Holdco, LLC. We also issued time-vested common units and incentive units to each of Drs. Haurwitz and May. Each of them then contributed all of their units to Caribou Therapeutics Holdco, LLC. All of these units held by Caribou Therapeutics Holdco, LLC were exchanged in the Reorganization for shares of junior preferred stock, shares of founder stock and shares of common stock. We also agreed to pay Caribou $5.0 million in service fees over the term of the services agreement and agreed to pay a percentage of Caribou's patent prosecution, filing and maintenance costs for such licensed intellectual property. As of December 31, 2015, we have paid $3.5 million to Caribou pursuant to the services agreement and $1.1 million for our portion of the patent prosecution, filing and maintenance costs pursuant to the license agreement.

**License and Collaborative Research Agreement with Novartis Institutes for BioMedical Research, Inc.**

In December 2014, we entered into a collaboration and license agreement, or the Novartis agreement, with Novartis Institutes for BioMedical Research, Inc., or Novartis, for the research of new CRISPR/Cas9-based therapies using CAR T cells and HSCs. We received a $10.0 million non-refundable upfront technology access payment from Novartis in January 2015 and are entitled to an additional $40.0 million, in aggregate, in additional technology access fees and research payments during the five-year collaboration term. In addition, we are eligible to receive 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. See the section entitled "Business—Collaborations—Novartis Institutes for BioMedical Research, Inc." appearing elsewhere in this prospectus for more information.

Novartis is a greater-than-5% stockholder in our company. Prior to our entry into the Novartis agreement, in September 2014, we entered into an agreement with Novartis for the exclusive right to negotiate a transaction involving our grant to Novartis of certain rights to our CRISPR/Cas9 technology. Pursuant to the exclusivity agreement, we agreed to issue to Novartis preferred units in exchange for a fee. We issued Novartis preferred

units, which converted into 4,761,905 shares of our Class A-1 preferred stock and 2,666,666 shares of our Class A-2 preferred stock in the Reorganization. Our preferred units were issued to Novartis pursuant to the terms of the September 2014 Unit Purchase Agreement described below.

**Private Placements of Securities**

***Class A/Junior Preferred Unit Financing of Intellia Therapeutics, LLC***

In July 2014, Intellia Therapeutics, LLC entered into an Equity Contribution and Unit Purchase Agreement among Atlas and Caribou, pursuant to which:

- Atlas contributed to Intellia Therapeutics, LLC $2,899,999 in cash and 1,000 shares of our common stock that were purchased for $100,000 in June 2014 in exchange for 2,857,142 Class A preferred units; and
- In exchange for 8,110,599 junior preferred units, Caribou, through its wholly owned, subsidiary, Caribou Therapeutics Holdco, LLC, contributed to us all of its membership interests of Intellia, LLC. Intellia, LLC was a holding company that was the original party to the license agreement with Caribou and otherwise had no other assets or operations prior to being merged with and into us in July 2014. See the section entitled "License Agreement and Services Agreement with Caribou Biosciences, Inc." for more information.

***Class A-1 Preferred Unit Financing of Intellia Therapeutics, LLC***

In September 2014, in connection with our Class A-1/A-2 preferred unit financing, we entered into a unit purchase agreement, or the Class A-1/A-2 purchase agreement, pursuant to which we agreed to issue and sell to investors an aggregate of (i) 5,714,287 Class A-1 preferred units at a purchase price of $1.05 for aggregate consideration of $6,000,001 and (ii) 3,999,999 Class A-2 preferred units at a purchase price of $1.50 for aggregate consideration of $5,999,999 at a subsequent closing. In December 2014, we amended the Class A-1/A-2 purchase agreement to provide for the issuance of the Class A-2 units at two subsequent closings.

The table below sets forth the aggregate number of Class A-1 preferred units sold to our directors, executive officers or holders of more than 5% of our capital stock at the time of such issuance, or an affiliate or immediate family member thereof under the Class A-1/A-2 purchase agreement:

| Name | Class A-1 Preferred Units | Total Purchase Price |
|---|---|---|
| Atlas Venture Fund IX, LP | 952,382 | $ 1,000,001 |
| Novartis Institutes for BioMedical Research, Inc | 4,761,905 | $ 5,000,000 |

***Class A-2 Preferred Unit Financing of Intellia Therapeutics, LLC***

The first subsequent closing under the Class A-1/A-2 purchase agreement, as amended, occurred in December 2014. The second subsequent closing under the Class A-1/A-2 purchase agreement, as amended, occurred in January 2015. The table below sets forth the number of Class A-2 preferred units sold to our directors, executive officers or holders of more than 5% of our capital stock at the time of such issuance, or an affiliate or immediate family member thereof:

| Name | Class A-2 Preferred Units | Total Purchase Price |
|---|---|---|
| Atlas Venture Fund IX, LP | 1,333,333 | $ 2,000,000 |
| Novartis Institutes for BioMedical Research, Inc | 2,666,666 | $ 3,999,999 |

***Series B Preferred Stock Financing***

In August 2015, Intellia Therapeutics, Inc. entered into a Series B Preferred Stock Purchase Agreement pursuant to which we issued and sold an aggregate of 13,336,601 shares of our Series B preferred stock at a price per share of $5.25, for an aggregate purchase price of $70.0 million. The following table sets forth the number of shares of our Series B Preferred Stock that we issued to our 5% stockholders and their affiliates in this transaction:

| Name | Shares of Series B Preferred Stock | Total Purchase Price |
|---|---|---|
| Atlas Venture Fund IX, LP | 761,905 | $ 4,000,001 |
| Entities affiliated with Fidelity Management & Research LLC | 2,857,143 | $ 15,000,001 |
| Novartis Institutes for BioMedical Research, Inc | 761,905 | $ 4,000,001 |
| Entities affiliated with OrbiMed Advisors LLC | 3,730,618 | $ 19,585,745 |

**Relationship with Regeneron and Concurrent Private Placement**

In April 2016, we entered into a research collaboration and license agreement with Regeneron. See "Business—Collaborations—Regeneron Pharmaceuticals, Inc." Pursuant to that collaboration, we received an upfront payment of $75.0 million.

Regeneron has agreed to purchase $50.0 million of our common stock in a separate private placement concurrent with the completion of this offering at a price per share equal to the public offering price. The sale of such shares will not be registered under the Securities Act. The closing of this offering is not conditioned upon the closing of such concurrent private placement.

**Concurrent Private Placement with Novartis**

Novartis has agreed to purchase $5.0 million of our common stock in a separate private placement concurrent with the completion of this offering at a price per share equal to the public offering price. The sale of such shares will not be registered under the Securities Act. The closing of this offering is not conditioned upon the closing of such concurrent private placement.

**Investors' Rights Agreement**

In connection with our Series B Preferred Stock financing, on August 20, 2015, we entered into an investors' rights agreement with the holders of our Junior, Series A-1, Series A-2 and Series B Preferred Stock and certain key holders of our common stock, which agreement was amended in connection with the execution of our collaboration agreement with Regeneron and in connection with Novartis' concurrent private placement. This agreement provides these holders with certain rights relating to the registration of their shares under the Securities Act. For a more detailed description of these registration rights, see the section titled "Description of Capital Stock—Registration Rights."

This agreement also establishes certain "information and observer" rights and rights of first offer, and sets forth certain covenants relating to insurance, employee agreements, employee stock, indemnification, and related matters. On the closing of this offering, all provisions relating to these rights and covenants will terminate.

**Consulting Arrangement**

From inception through September 30, 2014, we received consulting and management services from Atlas Venture Advisors, Inc., or Atlas Venture Advisors, which through its affiliate, Atlas Venture Fund IX, has a greater than 5% ownership interest in us. We have paid Atlas Venture Advisors $0.3 million for these services, including the reimbursement of expenses. We did not and do not have a written agreement in place with Atlas Venture Advisors with respect to the provision of consulting and management services, nor did or do we have a

written agreement in place for the use of Atlas Venture Advisors' premises. From time to time and at our request, partners and associates of Atlas Venture Advisors provided us with certain strategic and ordinary course business operations consulting services at fees mutually agreed upon in advance by us and Atlas Venture Advisors. For example, prior to becoming a consultant and then employee of our company, Atlas Venture Advisors provided us with the services of Nessan Bermingham, who is our Founder, President and Chief Executive Officer and who provided scientific leadership, business development and executive services. We paid these consulting and management services fees to Atlas Venture Advisors pursuant to invoices that Atlas Venture Advisors submitted to us from time to time. The consulting and management services fees paid to Atlas Venture Advisors were based upon customary rates for such services and did not exceed 5% of the consolidated gross revenue of Atlas Venture Advisors during any of the past three fiscal years.

**Indemnification Agreements**

We have entered into agreements to indemnify our directors and executive officers. These agreements will, among other things, require us to indemnify these individuals for certain expenses (including attorneys' fees), judgments, fines and settlement amounts reasonably incurred by such person in any action or proceeding, including any action by or in our right, on account of any services undertaken by such person on behalf of our company or that person's status as a member of our board of directors to the maximum extent allowed under Delaware law.

**Participation in this Offering**

We expect that certain of our existing stockholders, including certain affiliates of our directors, will purchase an aggregate of $45.6 million of shares of our common stock in this offering at the initial public offering price.

**Policies for Approval of Related Party Transactions**

Our board of directors reviews and approves transactions with directors, officers and holders of five percent or more of our voting securities and their affiliates, each a related party. Prior to this offering, the material facts as to the related party's relationship or interest in the transaction are disclosed to our board of directors prior to their consideration of such transaction, and the transaction is not considered approved by our board of directors unless a majority of the directors who are not interested in the transaction approve the transaction. Further, when stockholders are entitled to vote on a transaction with a related party, the material facts of the related party's relationship or interest in the transaction are disclosed to the stockholders, who must approve the transaction in good faith.

In connection with this offering, we have adopted a written related party transactions policy that such transactions must be approved by our audit committee. This policy became effective on the date on which the registration statement of which this prospectus is part is declared effective by the SEC.

## PRINCIPAL STOCKHOLDERS

The following table sets forth certain information known to us regarding beneficial ownership of our capital stock as of March 31, 2016, as adjusted to reflect the sale of common stock offered by us in this offering, for:

- each person or group of affiliated persons known by us to be the beneficial owner of more than five percent of our capital stock;
- each of our named executive officers;
- each of our directors; and
- all of our executive officers and directors as a group.

To the extent that the underwriters sell more than 6,000,000 shares in this offering, the underwriters have the option to purchase up to an additional 900,000 shares at the initial public offering price less the underwriting discount.

Beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power with respect to securities. Under those rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power. Except as noted by footnote, and subject to community property laws where applicable, we believe, based on the information provided to us, that the persons and entities named in the table below have sole voting and investment power with respect to all common stock shown as beneficially owned by them.

We expect that certain of our existing stockholders, including certain affiliates of our directors, will purchase an aggregate of $45.6 million of shares of our common stock in this offering at the initial public offering price. The information set forth in the table below does not reflect any purchase of any shares in this offering by such parties.

The percentage of beneficial ownership prior to this offering in the table below is based on 26,040,711 shares of common stock deemed to be outstanding as of March 31, 2016, assuming the conversion of all outstanding shares of our preferred stock upon the closing of this offering. The percentage of beneficial ownership after this offering in the table below is based on 35,096,265 shares of common stock assumed to be outstanding after the closing of the offering and concurrent private placements. All of our preferred stock convert into shares of common stock on a one-for-0.6465903 basis. The information in the table below assumes no exercise of the underwriters' option to purchase additional shares.

| Name and Address of Beneficial Owner(1) | Shares Beneficially Owned Prior to Offering | | Shares Beneficially Owned After Offering | |
|---|---|---|---|---|
| | Number | Percentage | Number | Percentage |
| **5% Stockholders:** | | | | |
| Atlas Venture Fund IX, L.P.(2) | 4,429,788 | 17.0% | 4,429,788 | 12.6% |
| Caribou Therapeutics Holdco, LLC(3) | 5,593,846 | 21.5% | 5,593,846 | 15.9% |
| Entities affiliated with Fidelity Management & Research Company(4) | 1,847,395 | 7.1% | 1,847,395 | 5.3% |
| Novartis Institutes for BioMedical Research, Inc.(5) | 5,295,881 | 20.3% | 5,573,658 | 15.9% |
| Entities affiliated with OrbiMed Advisors LLC(6) | 2,412,180 | 9.3% | 2,412,180 | 6.9% |
| Regeneron Pharmaceuticals, Inc(7) | — | — | 2,777,777 | 7.9% |
| **Named Executive Officers and Directors:** | | | | |
| Nessan Bermingham, Ph.D.(8) | 786,633 | 3.0% | 786,633 | 2.2% |
| Caroline Dorsa | — | — | — | — |
| Jean-François Formela, M.D.(9) | — | — | — | — |
| Carl L. Gordon, Ph.D., CFA(10) | 2,412,180 | 9.3% | 2,412,180 | 6.9% |
| Rachel E. Haurwitz, Ph.D.(11) | 5,593,846 | 21.5% | 5,593,846 | 15.9% |
| Perry Karsen | — | — | — | — |
| John M. Leonard, Ph.D.(12) | 524,420 | 2.0% | 524,420 | 1.5% |
| José E. Rivera, J.D.(13) | 262,210 | 1.0% | 262,210 | * |
| Sapna Srivastava, Ph.D.(14) | 159,031 | * | 159,031 | * |
| **All executive officers and directors as a group (11 persons)** | 10,087,934 | 38.7% | 10,087,934 | 28.7% |

* Represents beneficial ownership of less than one percent of our outstanding common stock

(1) Unless otherwise indicated, the address for each beneficial owner is c/o Intellia Therapeutics, Inc., 130 Brookline Street, Suite 201, Cambridge, MA 02139.

(2) Consists of (i) 611,827 shares of common stock issuable upon conversion of shares of Founder Stock, which are fully vested, (ii) 2,463,201 shares of common stock issuable upon conversion of shares of Series A-1 Preferred Stock, (iii) 862,120 shares of common stock issuable upon conversion of shares of Series A-2 Preferred Stock, and (iv) 492,640 shares of common stock issuable upon conversion of shares of Series B Preferred Stock. All shares are held directly by Atlas Venture Fund IX, L.P., or Atlas Venture Fund IX. Atlas Venture Associates IX, L.P., or AVA IX LP, is the general partner of Atlas Venture Fund IX, and Atlas Venture Associates IX, LLC, or AVA IX LLC, is the general partner of AVA IX LP. Peter Barrett, Bruce Booth, Jean-Francois Formela, Jeff Fagnan, Chris Lynch and Ryan Moore are the members of AVA IX LLC and collectively make investment decisions on behalf of Atlas Venture Fund IX. Dr. Formela is also a member of our board of directors. The address for Atlas Venture Fund IX, is 25 First Street, Suite 303, Cambridge, MA 02141.

(3) Consists of (i) an aggregate of 174,806 shares of restricted common stock and 174,806 shares of common stock issuable upon conversion of shares of Founder Stock, all of which was subsequently transferred to Caribou Therapeutics Holdco, LLC, or Caribou Holdco (See the section entitled “Certain Relationships and Related Party Transactions—License Agreement and Services Agreement with Caribou Biosciences, Inc.” for additional information) and all of which are subject to vesting requirements, and (ii) 5,244,234 shares of common stock issuable upon conversion of shares of Junior Preferred Stock. Rachel Haurwitz, a greater than 5% stockholder of Caribou, is the President, Chief Executive Officer and a director of Caribou. Caribou Holdco is a wholly-owned subsidiary of Caribou, and Dr. Haurwitz may be deemed to share voting and dispositive power with respect to the shares held by Caribou Holdco. Dr. Haurwitz is a member of our board of directors. Dr. Haurwitz disclaims beneficial ownership of such shares, except to the extent of her pecuniary interest therein, if any. The address for Caribou Therapeutics Holdco, LLC, or Caribou Holdco, is 2929 7th Street, Suite 120, Berkeley, CA 94710.

(4) Consists of (i) 328,993 shares of common stock issuable upon conversion of Series B Preferred Stock held by Fidelity Select Portfolios: Biotechnology Portfolio, (ii) 78,635 shares of common stock issuable upon conversion of Series B Preferred Stock held by Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund, (iii) 18,368 shares of common stock issuable upon conversion of Series B Preferred Stock held by Pyramis Lifecycle Blue Chip Growth Commingled Pool, (iv) 409,999 shares of common stock issuable upon conversion of Series B Preferred Stock held by Fidelity Securities Fund: Fidelity Blue Chip Growth Fund, (v) 2,707 shares of common stock issuable upon conversion of Series B Preferred Stock held by Fidelity Blue Chip Growth Commingled Pool, (vi) 128,357 shares of common stock issuable upon conversion of Series B Preferred Stock held by Fidelity Securities Fund: Fidelity Series Blue Chip Growth Fund, (vii) 107,438 shares of common stock issuable upon conversion of Series B Preferred Stock held by Fidelity Mt. Vernon Street Trust: Fidelity Series Growth Company Fund, (viii) 390,900 shares of common stock issuable upon conversion of Series B Preferred Stock held by Fidelity Mt. Vernon Street: Fidelity Growth Company Fund, (ix) 117,460 shares of common stock issuable upon conversion of

Series B Preferred Stock held by Fidelity Growth Company Commingled Pool, (x) 260,358 shares of common stock issuable upon conversion of Series B Preferred Stock held by Fidelity Securities Fund: Fidelity OTC Portfolio, (xi) 4,180 shares of common stock issuable upon conversion of Series B Preferred Stock held by Fidelity OTC Commingled Pool. These accounts are managed by direct or indirect subsidiaries of Fidelity Management and Research LLC, or FMR LLC. Edward C. Johnson 3d is a Director and the Chairman of FMR LLC and Abigail P. Johnson is a Director, the Vice Chairman and the President of FMR LLC. Members of the family of Edward C. Johnson 3d, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act, or Fidelity Funds, advised by Fidelity Management & Research Company, or FMR Co., a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Boards of Trustees. FMR Co. carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees. The address for FMR Co. is 245 Summer Street, Boston, MA 02110.

(5) Consists of (i) 3,079,001 shares of common stock issuable upon conversion of shares of Series A-1 Preferred Stock, (ii) 1,724,240 shares of common stock issuable upon conversion of shares of Series A-2 Preferred Stock, and (iii) 492,640 shares of common stock issuable upon conversion of shares of Series B Preferred Stock. All shares are held by Novartis Institutes for BioMedical Research, Inc., or Novartis. In addition, Novartis has agreed to purchase $5.0 million of our common stock in a concurrent private placement at a price per share equal to the public offering price. Shares beneficially owned after offering for Novartis reflect the purchase of such shares in the concurrent private placement at $18.00 per share. Novartis is an indirect wholly-owned subsidiary of, and controlled by, Novartis AG. The address for Novartis is 250 Massachusetts Avenue, Cambridge, MA 02139.

(6) Consists of (i) 1,847,400 shares of common stock issuable upon the conversion of shares of Series B Preferred Stock, held by OrbiMed Private Investments V, LP, or OPI V, and (ii) 564,780 shares of common stock issuable upon the conversion of shares of Series B Preferred Stock, held by OrbiMed Global Healthcare Master Fund, L.P., or OGH. OrbiMed Capital GP V LLC, or GP V, is the general partner of OPI V, and OrbiMed Global Healthcare GP LLC, or OGH GP, is the general partner of OGH. OrbiMed Advisors LLC, or OrbiMed, is the managing member of each of GP V and OGH GP. Samuel D. Isaly is the managing member of and owner of a controlling interest in OrbiMed. By virtue of such relationships, GP V, OrbiMed and Mr. Isaly may be deemed to have voting and investment power with respect to the shares held by OPI V and as a result may be deemed to have beneficial ownership of such shares, and OGH GP, OrbiMed and Mr. Isaly may be deemed to have voting and investment power with respect to the shares held by OGH and as a result may be deemed to have beneficial ownership of such shares. Dr. Carl L. Gordon, one of our board members, is a member of OrbiMed. Each of GP V, OGH GP, OrbiMed, Mr. Isaly and Dr. Gordon disclaims beneficial ownership of the shares held by OPI V and OGH, respectively, except to the extent of its or his pecuniary interest therein, if any. The address for these entities is 601 Lexington Avenue, 54th floor, New York, New York 10022.

(7) Regeneron Pharmaceuticals, Inc., or Regeneron, has agreed to purchase $50.0 million of our common stock in a concurrent private placement at a price per share equal to the public offering price. Shares beneficially owned after offering for Regeneron reflect the purchase of such shares in the concurrent private placement at $18.00 per share.

(8) Consists of (i) 349,614 shares of common stock, which are subject to vesting requirements, and (ii) 437,019 shares of common stock issuable upon conversion of shares of Founder Stock, which are subject to vesting requirements.

(9) See note (2) above.

(10) Consists of the shares listed in footnote (6) above. Dr. Gordon is a member of OrbiMed, which is the managing member of the general partner of OPI V, and the general partner of OGH, and as such Dr. Gordon may be deemed to share voting and investment power with respect to the shares held by such entities. Dr. Gordon disclaims beneficial ownership of these shares except to the extent of this pecuniary interest therein if any. Dr. Gordon's business address is 601 Lexington Avenue, 54th floor, New York, New York 10022.

(11) Consists of the shares listed in footnote (3) above. Dr. Haurwitz is the President, Chief Executive Officer, a director and greater than 5% stockholder of Caribou, the parent of Caribou Holdco. As such, Dr. Haurwitz may be deemed to share voting and dispositive power with respect to all shares held by such entity. Dr. Haurwitz disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Dr. Haurwitz's business address is 2929 7th Street, Suite 120, Berkeley, CA 94710.

(12) Consists of 524,420 shares of common stock, which are subject to vesting requirements.

(13) Consists of 262,210 shares of common stock, which are subject to vesting requirements. All shares are held by Rivak Capital LLC, or Rivak. Mr. Rivera is a member and manager of Rivak and has voting and dispositive power over the shares. The address for Rivak is 13450 N. Reigate Lane, Green Oaks, IL 60048.

(14) Consists of 159,031 shares of common stock, which are subject to vesting requirements.

## DESCRIPTION OF CAPITAL STOCK

*The following descriptions are summaries of the material terms of our amended and restated certificate of incorporation, which will be effective upon the closing of this offering and amended and restated bylaws, which became effective upon the effectiveness of the registration statement of which this prospectus is a part. The descriptions of the common stock and preferred stock give effect to changes to our capital structure that will occur immediately prior to the completion of this offering. We refer in this section to our amended and restated certificate of incorporation as our certificate of incorporation, and we refer to our amended and restated bylaws as our bylaws.*

### General

Upon completion of this offering, our authorized capital stock will consist of 120,000,000 shares of common stock, par value $0.0001 per share, and 5,000,000 shares of preferred stock, par value $0.0001 per share, all of which shares of preferred stock will be undesignated.

As of May 4, 2016, 26,040,711 shares of our common stock were outstanding and held by 71 stockholders of record. This amount assumes the conversion of all outstanding shares of our preferred stock into common stock, which will occur immediately prior to the closing of this offering.

### Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. The shares to be issued by us in this offering will be, when issued and paid for, validly issued, fully paid and non-assessable.

### Preferred Stock

Immediately prior to the completion of this offering, all outstanding shares of our preferred stock will be converted into shares of our common stock. Upon the consummation of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. Immediately after consummation of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

### Registration Rights

Upon the completion of this offering and the concurrent private placements, the holders of 25,051,650 shares of our common stock, including those issuable upon the conversion of preferred stock, will be entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of an investors' rights agreement between us, holders of our preferred stock and certain

holders our common stock, which agreement was amended to grant Regeneron and Novartis registration rights upon the completion of the concurrent private placements. The investors' rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations under this agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

***Demand Registration Rights***

Beginning 180 days after the completion of this offering, the holders of 25,051,650 shares of our common stock, including those issuable upon the conversion of shares of our preferred stock upon closing of this offering, are entitled to demand registration rights. Under the terms of the investor rights agreement, we will be required, upon the written request of holders of these securities that would result in an aggregate offering price of at least $10.0 million, to file a registration statement and use commercially reasonable efforts to effect the registration of all or a portion of these shares for public resale. We are required to effect only two registrations pursuant to this provision of the investor rights agreement.

***Short-Form Registration Rights***

Upon the completion of this offering, the holders of 25,051,650 shares of our common stock, including those issuable upon the conversion of shares of our preferred stock upon closing of this offering, are also entitled to short form registration rights. Pursuant to the investor rights agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of 20% in interest of these holders to sell registrable securities at an aggregate price of at least $4.0 million, we will be required to use commercially reasonable efforts to effect a registration of such shares. We are required to effect only two registrations in any twelve month period pursuant to this provision of the investor rights agreement.

***Piggyback Registration Rights***

Upon the completion of this offering, the holders of 25,051,650 shares of our common stock, including those issuable upon the conversion of shares of our preferred stock upon closing of this offering, are entitled to piggyback registration rights. If we register any of our securities either for our own account or for the account of other security holders, the holders of these shares are entitled to include their shares in the registration. Subject to certain exceptions contained in the investor rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

***Indemnification***

Our investor rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

***Expiration of Registration Rights***

The demand registration rights and short form registration rights granted under the investor rights agreement will terminate on the fifth anniversary of the completion of this offering.

**Anti-Takeover Effects of our Certificate of Incorporation and Bylaws and Delaware Law**

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

***Board Composition and Filling Vacancies***

Our certificate of incorporation provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

***No Written Consent of Stockholders***

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

***Meetings of Stockholders***

Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

***Advance Notice Requirements***

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

***Amendment to Certificate of Incorporation and Bylaws***

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, limitation of liability, the exclusive jurisdiction of the Delaware courts and the amendment of our bylaws and certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

***Undesignated Preferred Stock***

Our certificate of incorporation provides for 5,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

**Section 203 of the Delaware General Corporation Law**

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

**NASDAQ Global Market Listing**

Our common stock has been approved for listing on The NASDAQ Global Market under the trading symbol “NTLA.”

**Transfer Agent and Registrar**

The transfer agent and registrar for our common stock is Computershare Trust Company N.A.

## SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our shares. Future sales of our common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Based on the number of shares outstanding as of March 31, 2016, upon the completion of this offering and the concurrent private placements to Regeneron and Novartis, 35,096,265 shares of our common stock will be outstanding, assuming no exercise of the underwriters' option to purchase additional shares, no exercise of outstanding options and the issuance of 3,055,554 shares of common stock offered by us in the concurrent private placements, at a purchase price of $18.00 per share. Of the outstanding shares, all of the shares sold in this offering will be freely tradable, except that any shares held by our affiliates, as that term is defined in Rule 144 under the Securities Act, may only be sold in compliance with the limitations described below. All remaining shares of common stock held by existing stockholders immediately prior to the completion of this offering and any shares held by Regeneron and Novartis, including those sold to such parties in the concurrent private placement, will be "restricted securities" as such term is defined in Rule 144. These restricted securities were issued and sold by us, or will be issued and sold by us, in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, summarized below.

### Rule 144

In general, a person who has beneficially owned restricted stock for at least six months would be entitled to sell their securities provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, a sale and (ii) we are subject to the Securities Exchange Act of 1934, as amended, or the Exchange Act, periodic reporting requirements for at least 90 days before the sale. Persons who have beneficially owned restricted shares for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares then outstanding, which will equal approximately 350,963 shares immediately after this offering and the concurrent private placements, assuming no exercise of the underwriters' option to purchase additional shares, based on the number of shares outstanding as of March 31, 2016; or
- the average weekly trading volume of our common stock on The NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale;

provided, in each case, that we are subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Such sales both by affiliates and by non-affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

### Rule 701

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares.

However, substantially all Rule 701 shares are subject to lock-up agreements as described below and under "Underwriting" included elsewhere in this prospectus and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

**Lock-Up Agreements**

All of our directors, executive officers and stockholders have signed a lock-up agreement which prevents them from selling any of our common stock or any securities convertible into or exercisable or exchangeable for common stock for a period of not less than 180 days from the date of this prospectus without the prior written consent of the representatives, subject to certain exceptions. See the section entitled "Underwriting" appearing elsewhere in this prospectus for more information.

**Registration Rights**

Upon completion of this offering and the concurrent private placements, certain holders of our securities will be entitled to various rights with respect to registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See the section entitled "Description of Capital Stock—Registration Rights" appearing elsewhere in this prospectus for more information.

**Equity Incentive Plans**

We intend to file one or more registration statements on Form S-8 under the Securities Act to register our shares issued or reserved for issuance under our equity incentive plans. The first such registration statement is expected to be filed soon after the date of this prospectus and will automatically become effective upon filing with the SEC. Accordingly, shares registered under such registration statement will be available for sale in the open market, unless such shares are subject to vesting restrictions with us or the lock-up restrictions described above. As of April 22, 2016, we estimate that such registration statement on Form S-8 will cover approximately 7,499,999 shares.

## CERTAIN MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following is a general discussion of the material U.S. federal income tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes:

- a non-resident alien individual;
- a foreign corporation or any other foreign organization taxable as a corporation for U.S. federal income tax purposes or;
- a foreign estate or trust, the income of which is not subject to U.S. federal income tax on a net income basis.

This discussion does not address the tax treatment of partnerships or other entities that are past-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated hereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset within the meaning of Section 1221 of the Code, generally property held for investment.

This discussion does not address all aspects of U.S. federal income that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of any U.S. federal tax other than the income tax, U.S. state, local or non-U.S. taxes, the alternative minimum tax, or the Medicare tax on net investment income. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt or governmental organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;
- pension plans;
- controlled foreign corporations;
- passive foreign investment companies;
- persons that have a functional currency other than the U.S. dollar;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;

- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- persons for whom our stock constitutes "qualified small business stock" within the meaning of Section 1202 of the Code; and
- certain U.S. expatriates.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

**Distributions on Our Common Stock**

Distributions, if any, on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "Gain on sale, exchange or other disposition of our common stock." Any such distributions will also be subject to the discussion below under the section titled "Withholding and Information Reporting Requirements—FATCA."

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence. Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing a U.S. tax return with the IRS.

**Gain on Sale, Exchange or Other Disposition of Our Common Stock**

In general, a non-U.S. holder will not be subject to any U.S. federal income tax on any gain realized upon such holder's sale, exchange or other disposition of shares of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed-base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on Our Common Stock" also may apply;

- the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States, provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses); or
- we are, or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation," unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. If we are determined to be a U.S. real property holding corporation and the foregoing exception does not apply, then a purchaser may withhold 10% of the proceeds payable to a non-U.S. holder from a sale of our common stock and the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

**Backup Withholding and Information Reporting**

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in "Distributions on Our Common Stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

**Withholding and Information Reporting Requirements—FATCA**

The Foreign Account Tax Compliance Act, or FATCA, generally imposes a U.S. federal withholding tax at a rate of 30% on payments of dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," such foreign entity

undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. Under applicable U.S. Treasury regulations, withholding under FATCA currently applies to payments of dividends on our common stock, but will only apply to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2016. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of the tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

## UNDERWRITING

Under the terms and subject to the conditions contained in an underwriting agreement dated , 2016, we have agreed to sell to the underwriters named below, for whom Credit Suisse Securities (USA) LLC, Jefferies LLC and Leerink Partners LLC are acting as representatives, the following respective numbers of shares of common stock:

| Underwriter | Number of Shares |
|---|---|
| Credit Suisse Securities (USA) LLC | 2,100,000 |
| Jefferies LLC | 1,800,000 |
| Leerink Partners LLC | 1,800,000 |
| Wedbush Securities Inc | 300,000 |
| Total | 6,000,000 |

The underwriting agreement provides that the underwriters are obligated to purchase all the shares of common stock in the offering if any are purchased, other than those shares covered by the over-allotment option described below. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may be increased or the offering may be terminated.

We have granted to the underwriters a 30-day option to purchase on a pro rata basis up to 900,000 additional shares at the initial public offering price less the underwriting discounts and commissions. The option may be exercised only to cover any over-allotments of common stock.

The underwriters propose to offer the shares of common stock initially at the public offering price on the cover of this prospectus and to selling group members at that price less a selling concession of $0.756 per share. The underwriters may allow a discount of $0.252 per share on sales to other broker-dealers. After the initial public offering the representatives may change the public offering price and concession and discount to other broker-dealers.

The following table summarizes the compensation we will pay:

| | Per Share | | Total | |
|---|---|---|---|---|
| | Without Over-allotment | With Over-allotment | Without Over-allotment | With Over-allotment |
| Underwriting discounts and commissions paid by us | $ 1.26 | $ 1.26 | $7,560,000 | $8,694,000 |

We estimate that our out-of-pocket expenses for this offering (not including any underwriting discounts and commissions) will be approximately $2.6 million. We have agreed to reimburse the underwriters for expenses of approximately $50,000 related to the clearance of this offering with the Financial Industry Regulatory Authority.

The underwriters have informed us that they do not expect sales to accounts over which the underwriters have discretionary authority to exceed 5% of the shares of common stock being offered.

We have agreed that we will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, or file with the Securities and Exchange Commission a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, without the prior written consent of Credit Suisse Securities (USA) LLC, Jefferies LLC and Leerink Partners LLC for a period of 180 days after the date of this prospectus. The restrictions described in this paragraph do not apply in certain circumstances, including grants of employee stock options pursuant to our existing plans or issuances pursuant to the exercise of such employee options.

Our officers and directors and other stockholders and optionholders have agreed that they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, enter into a transaction that would have the same effect, or enter into any swap, hedge or other arrangement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock, whether any of these transactions are to be settled by delivery of our common stock or other securities, in cash or otherwise, or publicly disclose the intention to make any offer, sale, pledge or disposition, or to enter into any transaction, swap, hedge or other arrangement, without, in each case, the prior written consent of Credit Suisse Securities (USA) LLC, Jefferies LLC and Leerink Partners LLC for a period of 180 days after the date of this prospectus.

We have agreed to indemnify the underwriters against liabilities under the Securities Act, or contribute to payments that the underwriters may be required to make in that respect.

Our common stock has been approved for listing on The NASDAQ Global Market under the symbol "NTLA."

Prior to the offering, there has been no public market for our common stock. The initial public offering price will be determined through negotiations between us and the representatives. In determining the initial public offering price, we and the representatives expect to consider a number of factors including:

- the information set forth in this prospectus and otherwise available to the underwriters;
- our prospects and the history and prospects for the industry in which we compete;
- an assessment of our management;
- our prospects for future earnings;
- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies;
- the general condition of the securities markets at the time of the offering; and
- other factors deemed relevant by the underwriters and us.

Neither we nor the underwriters can assure investors that an active trading market will develop for our common stock, or that shares of our common stock will trade in the public market at or above the initial public offering price.

In connection with the offering the underwriters may engage in stabilizing transactions, over-allotment transactions, syndicate covering transactions, penalty bids and passive market making in accordance with Regulation M under the Exchange Act.

- Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum.
- Over-allotment transactions involve sales by the underwriters of shares in excess of the number of shares the underwriters are obligated to purchase, creating a syndicate short position. The short position may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the over-allotment option. In a naked short position, the number of shares involved is greater than the number of shares in the over-allotment option. The underwriters may close out any covered short position by either exercising their over-allotment option and/or purchasing shares in the open market.

- Syndicate covering transactions involve purchases of the common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option. If the underwriters sell more shares than could be covered by the over-allotment option, a naked short position, the position can only be closed out by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there could be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.
- Penalty bids permit the representative to reclaim a selling concession from a syndicate member when the common stock originally sold by the syndicate member is purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.
- In passive market making, market makers in the common stock who are underwriters or prospective underwriters may, subject to limitations, make bids for or purchases of our common stock until the time, if any, at which a stabilizing bid is made.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of the common stock. As a result the price of our common stock may be higher than the price that might otherwise exist in the open market. These transactions may be effected on The NASDAQ Global Market or otherwise and, if commenced, may be discontinued at any time.

A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters, or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make Internet distributions on the same basis as other allocations.

**Other Relationships**

Certain of the underwriters and their affiliates may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they may receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future. The underwriters are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. We have entered into an agreement with Wedbush Securities Inc., an underwriter in this offering, for advisory services pursuant to which Wedbush Securities Inc. will receive an agreed-upon fee not to exceed 0.35% of the net proceeds from this offering. In addition, Leerink Partners LLC, an underwriter in this offering, was the placement agent in our Series B financing in August 2015. Affiliates of Leerink Partners LLC were also investors in our Series B financing.

**Selling Restrictions**

***Notice to Prospective Investors in Australia***

This prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

1. You confirm and warrant that you are either:
   - a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;

- a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the Company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
- a person associated with the Company under Section 708(12) of the Corporations Act; or
- a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance.

2. You warrant and agree that you will not offer any of the securities issued to you pursuant to this prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

**Notice to Canadian Residents**

***Resale Restrictions***

The distribution of shares of common stock in Canada is being made only in the provinces of Ontario, Quebec, Alberta and British Columbia on a private placement basis exempt from the requirement that we prepare and file a prospectus with the securities regulatory authorities in each province where trades of these securities are made. Any resale of the common stock in Canada must be made under applicable securities laws which may vary depending on the relevant jurisdiction, and which may require resales to be made under available statutory exemptions or under a discretionary exemption granted by the applicable Canadian securities regulatory authority. Purchasers are advised to seek legal advice prior to any resale of the securities.

***Representations of Canadian Purchasers***

By purchasing shares of our common stock in Canada and accepting delivery of a purchase confirmation, a purchaser is representing to us and the dealer from whom the purchase confirmation is received that:

- the purchaser is entitled under applicable provincial securities laws to purchase the shares of common stock without the benefit of a prospectus qualified under those securities laws as it is an "accredited investor" as defined under National Instrument 45-106 – Prospectus Exemptions,
- the purchaser is a "permitted client" as defined in National Instrument 31-103 - Registration Requirements, Exemptions and Ongoing Registrant Obligations,
- where required by law, the purchaser is purchasing as principal and not as agent, and
- the purchaser has reviewed the text above under Resale Restrictions.

***Conflicts of Interest***

Canadian purchasers are hereby notified that the underwriters are relying on the exemption set out in section 3A.3 or 3A.4, if applicable, of National Instrument 33-105 – *Underwriting Conflicts* from having to provide certain conflict of interest disclosure in this document.

***Statutory Rights of Action***

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if the offering memorandum (including any amendment thereto) such as this document contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser of these securities in Canada should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

***Enforcement of Legal Rights***

All of our directors and officers as well as the experts named herein may be located outside of Canada and, as a result, it may not be possible for Canadian purchasers to effect service of process within Canada upon us or those persons. All or a substantial portion of our assets and the assets of those persons may be located outside of Canada and, as a result, it may not be possible to satisfy a judgment against us or those persons in Canada or to enforce a judgment obtained in Canadian courts against us or those persons outside of Canada.

***Taxation and Eligibility for Investment***

Canadian purchasers of our common stock should consult their own legal and tax advisors with respect to the tax consequences of an investment in the shares of common stock in their particular circumstances and about the eligibility of the shares of common stock for investment by the purchaser under relevant Canadian legislation.

***Notice to Prospective Investors in the European Economic Area***

In relation to each Member State of the European Economic Area that has implemented the Prospectus Directive, or each, a Relevant Member State, each underwriter represents and agrees that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, or the Relevant Implementation Date, it has not made and will not make an offer of our common stock to the public in that Relevant Member State prior to the publication of a prospectus in relation to our common stock that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of our common stock to the public in that Relevant Member State at any time:

- to any legal entity that is a qualified investor as defined in the Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the manager for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive;

provided that no such offer of our common stock shall require the publication by the issuer or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our common stock to be offered so as to enable an investor to decide to purchase or subscribe our common stock, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Member State and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including Directive 2010/73/EU, to the extent implemented in each Relevant Member State) and includes any relevant implementing measure in each Relevant Member State.

***Notice to Prospective Investors in Hong Kong***

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong ("SFO") and any rules made under that Ordinance; or in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong ("CO") or which do not constitute an offer or invitation to the public for the purpose of the CO or the SFO. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or

the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the SFO and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

***Notice to Prospective Investors in Japan***

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the prospectus will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

***Notice to Prospective Investors in Singapore***

This prospectus has not been and will not be lodged or registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares of common stock may not be circulated or distributed, nor may the common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares of common stock are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares of common stock pursuant to an offer made under Section 275 of the SFA except:

(i) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(ii) where no consideration is or will be given for the transfer;

(iii) where the transfer is by operation of law;

(iv) as specified in Section 276(7) of the SFA; or

(v) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

***Notice to Prospective Investors in Switzerland***

This document is not intended to constitute an offer or solicitation to purchase or invest in the securities described herein. The securities may not be publicly offered, sold or advertised, directly or indirectly, in, into or from Switzerland and will not be listed on the SIX Swiss Exchange or on any other exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the securities constitutes a prospectus as such term is understood pursuant to article 652a or article 1156 of the Swiss Code of Obligations or a listing prospectus within the meaning of the listing rules of the SIX Swiss Exchange or any other regulated trading facility in Switzerland, and neither this document nor any other offering or marketing material relating to the securities may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, nor the Company nor the securities have been or will be filed with or approved by any Swiss regulatory authority. The securities are not subject to the supervision by any Swiss regulatory authority, e.g., the Swiss Financial Markets Supervisory Authority FINMA (FINMA), and investors in the securities will not benefit from protection or supervision by such authority.

***Notice to Prospective Investors in the United Kingdom***

Each underwriter:

- has only communicated or caused to be communicated and will only communicate or cause to be communicated any invitation or inducement to engage in investment activity (within the meaning of section 21 of the Financial Services and Markets Act 2000, or the FSMA) in connection with the sale or issue of common stock in circumstances in which section 21 of the FSMA does not apply to such underwriter; and
- has complied with, and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of common stock in, from, or otherwise involving the United Kingdom.

This prospectus is directed solely at persons who (i) are outside the United Kingdom or (ii) have professional experience in matters relating to investments or (iii) are persons falling within Article 49(2)(a) to (d) of the FSMA (Financial Promotion) Order 2005 (all such persons together being referred to as "relevant persons"). This prospectus must not be acted on or relied on by persons who are not relevant persons. Any investment or investment activity to which this prospectus relates is available only to relevant persons and will be engaged in with relevant persons only.

## LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Certain legal matters related to this offering will be passed upon for the underwriters by Latham & Watkins LLP, Boston, Massachusetts.

## EXPERTS

The consolidated financial statements as of December 31, 2014 and 2015, and for the period from May 7, 2014 (inception) to December 31, 2014 and the year ended December 31, 2015, included in this prospectus, have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report appearing herein. Such consolidated financial statements have been so included in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

## CHANGE IN INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We dismissed PricewaterhouseCoopers LLP, or PwC, as our independent registered public accounting firm on November 11, 2015 effective as of that date. Our board of directors participated in and approved our change in independent registered public accounting firm. PwC issued their audit report, dated September 4, 2015, on our consolidated financial statements as of December 31, 2014 and for the period from May 7, 2014 (inception) to December 31, 2014. The report of PwC on our consolidated financial statements as of December 31, 2014 and for the period from May 7, 2014 (inception) to December 31, 2014 contained no adverse opinion or disclaimer of opinion and was not qualified or modified as to audit scope, accounting principle or uncertainty. During the period from May 7, 2014 (inception) to December 31, 2014 and the subsequent interim period through November 11, 2015, (i) there were no disagreements (as that term is used in Item 304(a)(1)(iv) of Regulation S-K and the related instructions) with PwC on any matter of accounting principles or practices, financial statement disclosure, or auditing scope or procedure, which disagreements if not resolved to the satisfaction of PwC would have caused PwC to make reference thereto in their report on our audited consolidated financial statements for the period from May 7, 2014 (inception) to December 31, 2014, and (ii) there were no "reportable events" as such term is defined in Item 304(a)(1)(v) of Regulation S-K.

We provided PwC with a copy of the disclosures set forth under the heading "Change in Independent Registered Public Accounting Firm" included in this prospectus and requested that PwC furnish a letter addressed to the Securities and Exchange Commission stating whether or not PwC agrees with statements related to them made by us in the disclosures above. PwC has furnished such letter dated December 22, 2015, a copy of which is filed as Exhibit 16.1 to the registration statement of which this prospectus forms a part.

We engaged Deloitte & Touche LLP, or Deloitte, as our independent registered public accounting firm on November 17, 2015. The decision to change our independent registered public accounting firm was approved by our board of directors. During the period from May 7, 2014 (inception) to December 31, 2014 and the subsequent period preceding our engagement of Deloitte as our independent registered public accounting firm on November 17, 2015, neither we nor anyone acting on our behalf consulted with Deloitte regarding: (1) the application of accounting principles to a specific completed or contemplated transaction; or the type of audit opinion that might be rendered on our consolidated financial statements and Deloitte did not provide any written report or oral advice that Deloitte concluded was an important factor considered by us in reaching a decision as to any such accounting, auditing or financial reporting issue; or (2) any matter that was either the subject of a disagreement, as that term is defined in S-K 304(a)(1)(iv) and the related instructions to S-K 304, or a reportable event, as that term is defined in S-K 304(a)(1)(v).

## WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 (File Number 333-210689) under the Securities Act with respect to the common stock we are offering by this prospectus. This prospectus does not contain all of the information included in the registration statement. For further information pertaining to us and our common stock, you should refer to the registration statement and to its exhibits. Whenever we make reference in this prospectus to any of our contracts, agreements or other documents, the references are not necessarily complete, and you should refer to the exhibits attached to the registration statement for copies of the actual contract, agreement or other document.

Upon the completion of the offering, we will be subject to the informational requirements of the Exchange Act and will file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, at the SEC's website at www.sec.gov. You may also read and copy any document we file with the SEC at its public reference facility at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. We also maintain a website at www.intelliatx.com. Upon completion of the offering, you may access, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendment to those reported filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC.

You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

## INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

We have audited the accompanying consolidated balance sheets of Intellia Therapeutics, Inc. (successor to Intellia Therapeutics, LLC) and subsidiaries (the "Company") as of December 31, 2014 and 2015, and the related consolidated statements of operations, convertible preferred stock and stockholders' equity (deficit), and cash flows for the period from May 7, 2014 (inception) to December 31, 2014 and the year ended December 31, 2015. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, 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. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of Intellia Therapeutics, Inc. and subsidiaries as of December 31, 2014 and 2015, and the results of their operations and their cash flows for the period from May 7, 2014 (inception) to December 31, 2014 and the year ended December 31, 2015, in conformity with accounting principles generally accepted in the United States of America.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 16, 2016 (April 25, 2016 as to the effects of the reverse stock split discussed in Note 2)

**INTELLIA THERAPEUTICS, INC. (SUCCESSOR TO INTELLIA THERAPEUTICS, LLC)**
**CONSOLIDATED BALANCE SHEETS**
**(in thousands, except unit, share and per share data)**

| | December 31, 2014 | December 31, 2015 | Pro Forma December 31, 2015 (unaudited) |
|---|---|---|---|
| **ASSETS** | | | |
| Current assets: | | | |
| Cash and cash equivalents | $ 9,845 | $ 75,816 | $ 75,816 |
| Accounts receivable | — | 1,000 | 1,000 |
| Prepaid expenses and other current assets | 285 | 810 | 810 |
| Total current assets | 10,130 | 77,626 | 77,626 |
| Property and equipment, net | 308 | 2,708 | 2,708 |
| Other assets | 256 | 1,805 | 1,805 |
| Total assets | $ 10,694 | $ 82,139 | $ 82,139 |
| **LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)** | | | |
| Current liabilities: | | | |
| Accounts payable | $ 199 | $ 1,360 | $ 1,360 |
| Accrued expenses | 2,156 | 2,788 | 2,788 |
| Current portion of deferred revenue | — | 6,547 | 6,547 |
| Total current liabilities | 2,355 | 10,695 | 10,695 |
| Deferred revenue, net of current portion | — | 3,765 | 3,765 |
| Other long-term liabilities | 773 | 323 | 323 |
| Commitments and contingencies (Note 6) | | | |
| Convertible preferred stock (Series B, Series A-2, Series A-1, Junior and Founder), $0.0001 par value; no shares authorized, issued or outstanding as of December 31, 2014 and 36,500,000 shares authorized and 36,316,628 shares issued and outstanding as of December 31, 2015; aggregate liquidation preference of $95,946 as of December 31, 2015; no shares issued and outstanding, pro forma as of December 31, 2015 (unaudited) | — | 88,557 | — |
| Stockholders' equity (deficit) | | | |
| Preferred units (Class A-2, Class A-1 and Junior), no par value; 19,348,694 and no units issued and outstanding as of December 31, 2014 and 2015, respectively; aggregate liquidation preference of $21,516 as of December 31, 2014 | 16,448 | — | — |
| Common units, no par value; 2,298,000 units and no units issued and outstanding as of December 31, 2014 and 2015, respectively | 607 | — | — |
| Incentive units, no par value; 1,558,498 and no units issued and outstanding as of December 31, 2014 and 2015, respectively | 50 | — | — |
| Common stock, $0.0001 par value; no shares authorized, issued or outstanding as of December 31, 2014 and 50,000,000 shares authorized and 2,558,755 shares issued and outstanding as of December 31, 2015; 26,040,711 shares issued and outstanding, pro forma as of December 31, 2015 (unaudited) | — | — | 3 |
| Additional paid-in capital | — | 735 | 89,289 |
| Accumulated deficit | (9,539) | (21,936) | (21,936) |
| Total stockholders' equity (deficit) | 7,566 | (21,201) | 67,356 |
| Total liabilities and stockholders' equity (deficit) | $ 10,694 | $ 82,139 | $ 82,139 |

The accompanying notes are an integral part of these consolidated financial statements.

**INTELLIA THERAPEUTICS, INC. (SUCCESSOR TO INTELLIA THERAPEUTICS, LLC)**
**CONSOLIDATED STATEMENTS OF OPERATIONS**
**(in thousands, except per unit and per share data)**

| | Period from May 7, 2014 (inception) to December 31, 2014 | Year Ended December 31, 2015 |
|---|---|---|
| Collaboration revenue | $ — | $ 6,044 |
| Operating expenses: | | |
| Research and development | 1,105 | 11,170 |
| In-process research and development | 6,055 | — |
| General and administrative | 2,379 | 8,283 |
| Total operating expenses | 9,539 | 19,453 |
| Loss before income taxes | (9,539) | (13,409) |
| Benefit from income taxes | — | 1,012 |
| Net loss | $ (9,539) | $ (12,397) |
| Net loss per common unit, basic and diluted | $ (11.55) | $ — |
| Net loss per share attributable to common stockholders, basic and diluted | $ — | $ (51.02) |
| Weighted average common units outstanding, basic and diluted | 826 | — |
| Weighted average shares outstanding, basic and diluted | — | 243 |
| Pro forma net loss per share, basic and diluted (unaudited) | | $ (0.70) |
| Pro forma weighted average shares outstanding, basic and diluted (unaudited) | | 17,664 |

The accompanying notes are an integral part of these consolidated financial statements.

**INTELLIA THERAPEUTICS, INC. (SUCCESSOR TO INTELLIA THERAPEUTICS, LLC)**
**CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)**
**(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' | Convertible Preferred Stock | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Units | Amount | Units | Amount | Shares | Amount | Units | Amount | Capital | Deficit | Equity | Shares | Amount |
| **Balance at May 7, 2014 (inception)** | — | $ — | — | $ — | — | $ — | — | $ — | $ — | $ — | $ — | — | $ — |
| Issuance of Junior Preferred Units in connection with the Caribou agreements | 8,110,599 | 4,055 | — | — | — | — | — | — | — | — | 4,055 | — | — |
| Issuance of Class A-1 and Class A-2 Preferred Units, net of issuance costs of $258 | 11,238,095 | 12,393 | — | — | — | — | — | — | — | — | 12,393 | — | — |
| Issuance of common units | — | — | 946,237 | 349 | — | — | — | — | — | — | 349 | — | — |
| Equity-based compensation | — | — | 1,351,763 | 258 | — | — | 1,558,498 | 50 | — | — | 308 | — | — |
| Net loss | — | — | — | — | — | — | — | — | — | (9,539) | (9,539) | — | — |
| **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 |

The accompanying notes are an integral part of these consolidated financial statements.

**INTELLIA THERAPEUTICS, INC. (SUCCESSOR TO INTELLIA THERAPEUTICS, LLC)**
**CONSOLIDATED STATEMENTS OF CASH FLOWS**
**(amounts in thousands)**

| | Period from May 7, 2014 (inception) to December 31, 2014 | Year Ended December 31, 2015 |
|---|---|---|
| **Cash flows from operating activities:** | | |
| Net loss | $ (9,539) | $ (12,397) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Acquired in-process research and development | 6,055 | — |
| Depreciation and amortization expense | 3 | 328 |
| Loss on disposal of property and equipment | — | 9 |
| Equity-based compensation expense | 308 | 1,308 |
| Benefit from intraperiod tax allocation | — | (1,012) |
| Changes in operating assets and liabilities: | | |
| Prepaid expenses and other current assets | (285) | (525) |
| Accounts payable | 163 | 335 |
| Accrued expenses | 1,056 | 805 |
| Deferred revenue | — | 9,312 |
| Other assets | (256) | (76) |
| Other long-term liabilities | 173 | 150 |
| Net cash used in operating activities | (2,322) | (1,763) |
| **Cash flows from investing activities:** | | |
| Purchases of property and equipment | (275) | (2,554) |
| Acquisition of in-process research and development | (300) | — |
| Net cash used in investing activities | (575) | (2,554) |
| **Cash flows from financing activities:** | | |
| Payments to acquire in-process research and development | — | (1,100) |
| Proceeds from sale of Class A-1 preferred units, Class A-2 preferred units and Series B preferred stock | 12,651 | 74,661 |
| Payment of preferred unit and preferred stock issuance costs | (258) | (2,671) |
| Proceeds from sale of common units | 349 | — |
| Payment of proposed public offering costs | — | (602) |
| Net cash provided by financing activities | 12,742 | 70,288 |
| **Net increase in cash and cash equivalents** | 9,845 | 65,971 |
| Cash and cash equivalents at beginning of period | — | 9,845 |
| Cash and cash equivalents at end of period | $ 9,845 | $ 75,816 |
| **Supplemental disclosure of noncash investing and financing activities:** | | |
| Purchases of property and equipment unpaid at period end | $ 36 | $ 219 |
| Financing costs incurred but unpaid at period end | — | 970 |
| Noncash portion of acquired in-process research and development | 4,055 | — |
| Acquisition of in-process research and development unpaid at period end | 1,700 | 600 |

The accompanying notes are an integral part of these consolidated financial statements.

**INTELLIA THERAPEUTICS, INC. (SUCCESSOR TO INTELLIA THERAPEUTICS, LLC)**
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**1. Nature of the Business**

Intellia Therapeutics was formed in May 2014 in the state of Delaware as AZRN, Inc. and amended its certificate of incorporation in July 2014 to change its name from AZRN, Inc. to Intellia Therapeutics, Inc. 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. There was no impact on the consolidated financial statements as a result of the Reorganization except for the reclassification of members' equity to stockholders' equity or temporary equity.

Intellia Therapeutics, LLC (collectively referred to with its wholly owned, controlled subsidiary, Intellia Therapeutics, Inc., as "Intellia" or the "Company") is a gene editing company focused on developing potentially curative therapeutics utilizing a recently developed biological tool known as CRISPR/Cas9.

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.

The accompanying financial statements have been prepared on a basis that assumes the Company will continue as a going concern and contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business. Through December 31, 2015, the Company has funded its operations with proceeds from the sale of capital stock and with payments received under its collaboration arrangement with Novartis Institutes for BioMedical Research, Inc. ("Novartis"). Since its inception, the Company has incurred recurring losses, including net losses of $9.5 million for the period from May 7, 2014 (inception) to December 31, 2014 and $12.4 million for the year ended December 31, 2015. The Company expects to continue to generate operating losses in the foreseeable future.

The Company expects that its cash and cash equivalents of $75.8 million as of December 31, 2015 will be sufficient to fund its operations for at least the next twelve months. The future of the Company beyond that point is largely dependent on its ability to finance its operations through additional capital raising transactions and collaborations. Although the Company has been successful in raising capital in the past, there is no assurance that additional funding will be available on acceptable terms, if at all. The Company may seek additional funding through sales of equity or convertible debt securities or additional collaboration agreements. The terms of any financing may adversely affect the holdings or the rights of the Company's security holders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting the Company's ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. The Company may not be able to enter into additional collaboration arrangements. The Company's inability to raise capital as and when needed could have a negative impact on its financial condition and ability to pursue its business strategies. The Company could be forced to curtail the development of a product candidate, reduce or delay its development program or one or more of its other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase its

expenditures and undertake development or commercialization activities at its own expense, which could adversely affect its business prospects.

**2. Summary of Significant Accounting Policies**

***Basis of Presentation***

The consolidated financial statements prior to the Reorganization include the accounts of Intellia Therapeutics, LLC and its wholly owned, controlled subsidiary, Intellia Therapeutics, Inc. The consolidated financial statements following the Reorganization 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.

The Company's Board of Directors and stockholders approved a one-for-1.7 reverse stock split of the Company's common stock that became effective on April 25, 2016. All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split.

***Unaudited Pro Forma Information***

On September 4, 2015, the Company's board of directors authorized the Company to file a confidential draft registration statement with the Securities and Exchange Commission to sell shares of its common stock to the public. Upon the closing of an initial public offering, all of the Company's outstanding shares of preferred stock will automatically convert into shares of common stock. The unaudited pro forma consolidated balance sheet information as of December 31, 2015 reflects the conversion of all outstanding shares of preferred stock into common stock upon the closing of an initial public offering.

For purposes of calculating pro forma basic and diluted loss per share, all shares of preferred stock outstanding as of December 31, 2015 have been treated as if they had been converted to common stock on May 7, 2014 (inception) or on the issuance date of the preferred stock, if later.

***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 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, the recognition of research and development expenses and the valuation of common and incentive units. 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.

***Subsequent Events***

The Company considers events or transactions that occur after the balance sheet date but before the financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The Company evaluated all events and transactions through March 16, 2016, the date the consolidated financial statements as of December 31, 2014 and 2015 were issued.

**INTELLIA THERAPEUTICS, INC. (SUCCESSOR TO INTELLIA THERAPEUTICS, LLC)**
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

***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 consisted primarily of cash equivalents, accounts receivable and accounts payable. As of December 31, 2015, the Company's financial assets recognized at fair value consisted of the following:

| | Fair Value as of December 31, 2015 | | | |
|---|---|---|---|---|
| | Total | Level 1 | Level 2 | Level 3 |
| | (in thousands) | | | |
| Cash equivalents .. | $30,000 | $30,000 | $ — | $ — |
| Total | $30,000 | $30,000 | $ — | $ — |

***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, 2015, cash equivalents consisted of interest-bearing money market accounts.

***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 operating accounts in excess of federally insured limits with financial institutions that management believes to be of high credit quality.

***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 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 group 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 impairment losses on long-lived assets.

***Deferred Issuance Costs***

Deferred issuance costs, which consist of direct incremental legal and professional accounting fees relating to the proposed public offering, are capitalized. The deferred issuance costs will be offset against public offering proceeds upon the consummation of the offering. In the event the offering is terminated, deferred issuance costs will be expensed. As of December 31, 2015, the Company capitalized $1.5 million of deferred issuance costs related to the proposed public offering, which are included in other long-term assets on the consolidated balance sheet.

***Income Taxes***

Intellia Therapeutics, LLC was a Delaware limited liability company for federal and state income tax purposes; therefore, the Company's taxable losses were allocated to the members in accordance with the LLC operating agreement. Accordingly, no federal or state income tax was assessed to Intellia Therapeutics, LLC; however Intellia Therapeutics, Inc. is subject to federal, state and local income taxes and is included in the consolidated tax position for all periods presented. Accordingly, the Reorganization and change in tax status of the reporting entity did not have an impact on the consolidated tax provision.

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.

**INTELLIA THERAPEUTICS, INC. (SUCCESSOR TO INTELLIA THERAPEUTICS, LLC)**
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

***Convertible Preferred Stock***

The Company classifies stock that is redeemable in circumstances outside of the Company's control outside of permanent equity. The Company records convertible preferred stock at fair value upon issuance, net of any issuance costs or discounts. No accretion has been recognized as the contingent events that could give rise to redemption are not deemed probable.

***Revenue Recognition***

The Company recognizes revenue for each 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 and comprehensive loss 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 performance obligations will be performed 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 the 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. 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 complete 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.

**INTELLIA THERAPEUTICS, INC. (SUCCESSOR TO INTELLIA THERAPEUTICS, LLC)**
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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 agreement, 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 collaboration. The Company's primary performance obligations under this collaboration 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 and recognizes equity-based compensation expense, net of estimated forfeitures, on a straight-line basis over the requisite service period of the awards, which is generally the vesting period of the respective award. Compensation expense is recognized for only the portion of awards that are expected to vest. In developing a forfeiture rate estimate, the Company has considered its historical experience to estimate pre-vesting forfeitures for service-based awards. The Company estimates forfeitures at the time of grant and revises those estimates in subsequent periods if actual forfeitures differ from those estimates.

The Company measures equity awards granted to consultants and non-employees based on the fair value of the award on the date of grant. 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 the common or incentive units.

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.

***Earnings (Loss) per Unit or Share***

The Company calculates basic earnings (loss) per common unit by dividing income (loss) allocable to common unitholders by the weighted average number of common units outstanding, calculates basic earnings (loss) per incentive unit by dividing income (loss) allocable to incentive unitholders by the weighted average number of incentive units outstanding and calculates basic earnings (loss) per share by dividing income (loss) 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 units, preferred stock, common units, common stock, incentive units 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 earnings (loss) per share after giving consideration to the dilutive effect of preferred units, preferred stock, common units, common stock, incentive units and restricted common stock that are outstanding during the period, except where such units 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 United States. To date, all of the Company's revenue has been generated in the United States from a single arrangement.

***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 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. The Company expects that 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. In July 2015, the FASB voted to delay the effective date of this standard such that ASU 2014-09 will be effective for the Company for annual periods beginning after December 15, 2017 and for interim periods within those fiscal years. Early adoption of the standard is permitted for annual periods beginning after December 15, 2016. The Company is evaluating the impact that the adoption of ASU 2014-09 will have on its consolidated financial statements.

In August 2014, the FASB issued ASU No. 2014-15*, Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern*. ASU 2014-15 amends Accounting Standards Codification ("ASC") 205-40,

**INTELLIA THERAPEUTICS, INC. (SUCCESSOR TO INTELLIA THERAPEUTICS, LLC)**
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*Presentation of Financial Statements—Going Concern*, by providing guidance on determining when and how reporting entities must disclose going-concern uncertainties in their financial statements, including requiring management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date of issuance of the entity's financial statements and providing certain disclosures if there is substantial doubt about the entity's ability to continue as a going concern. ASU 2014-15 will be effective for the Company for annual periods ending after December 15, 2016 and interim periods within annual periods beginning after December 15, 2016. The Company is evaluating the potential impact of this ASU on its consolidated financial statements but believes its adoption will have no impact on its financial position, results of operations or cash flows.

In February 2015, the FASB issued ASU No. 2015-02, *Consolidation (Topic 810)—Amendments to the Consolidation Analysis*. ASU 2015-02 modifies the existing consolidation guidance in ASC 810, *Consolidation*, by significantly changing the consolidation analysis reporting organizations are required to complete in determining whether to consolidate certain legal entities. ASU 2015-02 requires either a retrospective or modified retrospective approach to adoption and will be effective for the Company for annual periods beginning after December 15, 2015 and for interim periods within those fiscal years. The Company is evaluating the impact of the adoption of ASU 2015-02 on its consolidated financial statements but believes its adoption will have no material impact on its financial position, results of operations or cash flows.

In April 2015, the FASB issued ASU No. 2015-05, *Customer's Accounting for Fees Paid in a Cloud Computing Arrangement*. ASU 2015-05 amends ASC 350-40, *Internal-Use Software*, by providing customers with guidance on determining whether a cloud computing arrangement contains a software license that should be accounted for as internal-use software. ASU 2015-05 will be effective for the Company for annual periods beginning after December 15, 2015 and interim periods within annual periods beginning after December 15, 2016. The Company is evaluating the impact that this ASU may have on its consolidated financial statements, if any.

In November 2015, the FASB issued ASU No. 2015-17, *Balance Sheet Classification of Deferred Taxes*. ASU 2015-17 amends ASC 740, *Income Taxes*, by requiring entities to present deferred tax assets and deferred tax liabilities as noncurrent in a classified balance sheet. ASU 2015-17 would be effective for annual periods beginning after December 15, 2016 and interim periods within those fiscal years. Early adoption is permitted. The Company elected to early adopt this guidance on a prospective basis beginning with its year ending as of December 31, 2015; however there was no material impact to its financial position as the Company carries a full valuation allowance.

In February 2016, the FASB issued ASU 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 public companies for annual periods beginning after December 15, 2018 and interim periods within those fiscal years and for private companies for annual periods beginning after December 15, 2019 and interim periods within fiscal years beginning after December 15, 2020. The Company is evaluating the impact that the adoption of ASU 2016-02 will have on its consolidated financial statements.

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### 3. Property and Equipment, net

Property and equipment, net consisted of the following:

| | December 31, | |
|---|---|---|
| | 2014 | 2015 |
| | (in thousands) | |
| Laboratory equipment | $ 36 | $2,518 |
| Office furniture and equipment | 123 | 245 |
| Computer equipment | 77 | 121 |
| Leasehold improvements | 75 | 155 |
| Property and equipment | 311 | 3,039 |
| Less: Accumulated depreciation and amortization | (3) | (331) |
| Property and equipment, net | $308 | $2,708 |

Depreciation and amortization expense was $3,000 for the period from May 7, 2014 (inception) to December 31, 2014 and $0.3 million for the year ended December 31, 2015.

### 4. Accrued Expenses

Accrued expenses consisted of the following:

| | December 31, | |
|---|---|---|
| | 2014 | 2015 |
| | (in thousands) | |
| Employee compensation | $ 458 | $1,281 |
| In-process research and development obligation | 1,100 | 600 |
| Research and development and professional expenses | 598 | 907 |
| | $2,156 | $2,788 |

In July 2014, the Company entered into agreements with Caribou Biosciences, Inc. (“Caribou”), under which the Company received a license for certain patents and limited research and development services from Caribou. The in-process research and development obligation represents the portion of the Company’s obligation under these agreements that is attributable to the license. Refer to Note 6, *Commitments and Contingencies*, for additional information regarding these agreements.

### 5. Income Taxes

The Company did not record income tax benefits for the operating losses incurred during the periods presented due to its uncertainty of realizing a tax benefit from the deferred tax assets.

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 8, *Collaboration*, 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:

| | Period from May 7, 2014 (inception) to December 31, 2014 | Year Ended December 31, 2015 |
|---|---|---|
| Federal statutory income tax rate | (34.0)% | (34.0)% |
| State income taxes | (4.5) | (4.4) |
| Intraperiod tax allocation | — | (6.7) |
| Permanent items | 1.1 | 3.3 |
| Research and development tax credits | (0.6) | (1.8) |
| Change in valuation allowance | 38.0 | 36.0 |
| Effective income tax rate | —% | (7.6)% |

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

| | December 31, | |
|---|---|---|
| | 2014 | 2015 |
| | (in thousands) | |
| Deferred tax assets: | | |
| Intangibles, including acquired in-process research and development | $ 2,264 | $ 2,151 |
| Capitalized start-up costs | 745 | 830 |
| Net operating loss carryforwards | 495 | 4,653 |
| Research and development credit carryforwards | 59 | 418 |
| Accruals and allowances | 61 | 211 |
| Gross deferred tax assets | 3,624 | 8,263 |
| Deferred tax asset valuation allowance | (3,624) | (7,452) |
| Total deferred tax assets | — | 811 |
| Deferred tax liabilities: | | |
| Deferred revenue | — | (811) |
| Total deferred tax liabilities | — | (811) |
| Net deferred tax asset (liability) | $ — | $ — |

As of December 31, 2015, the Company had federal and state net operating loss carryforwards of $12.5 million and $9.4 million, respectively, which begin to expire in 2034. As of December 31, 2015, the Company had federal and state research and development tax credits carryforwards of approximately $0.3 million and $0.2 million, which begin to expire in 2034 and 2029, respectively.

The Company evaluated the expected realizability of its net deferred tax assets as of December 31, 2014 and 2015 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, 2014 and 2015. The valuation allowance increased by $3.6 million in 2014 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, 2015, the Company had not recorded any unrecognized tax benefits. The Company files income tax returns in the United States 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. There are currently no pending tax examinations.

**6. Commitments and Contingencies**

***Commitments***

*Caribou Agreement*

In July 2014, the Company entered into a license agreement with Caribou for an exclusive, worldwide license for a defined field of human therapeutic, prophylactic, and palliative uses, except for anti-fungal and anti-microbial uses, of any CRISPR/Cas9-related patents and applications owned, controlled or licensed by Caribou, as well as companion diagnostics to the Company's products or product candidates. This license agreement also includes any CRISPR/Cas9-related intellectual property developed by Caribou between July 16, 2014 and, at least, July 16, 2016 for the Company's field of use.

Pursuant to a services agreement entered into with Caribou contemporaneously with the Caribou license agreement, the Company is also receiving two years of research and development services from Caribou. Under the services agreement's research plan, Caribou primarily focuses on the improvement and further development of the CRISPR/Cas9 system and its components.

In exchange for 8,110,599 of the Company's Junior Preferred Units, Caribou, through its wholly owned subsidiary, Caribou Therapeutics Holdco, LLC, contributed to the Company all of its membership interests of Intellia, LLC. Intellia, LLC was a holding company that was the original party to the license agreement with Caribou and otherwise had no other assets or operations prior to being merged with and into the Company in July 2014. In addition, the Company is paying Caribou $5.0 million over the term of the two-year services agreement and agreed to pay 30.0% of Caribou's patent prosecution, filing, and maintenance costs for such licensed intellectual property under the license agreement, amounting to $1.1 million paid through December 31, 2015. The Company granted Caribou an exclusive, royalty-free, worldwide license to any CRISPR/Cas9 patents and know-how for research, development and commercialization activities in Caribou's retained field of use owned or developed by the Company between July 16, 2014 and, at least, July 16, 2016.

For the period from May 7, 2014 (inception) through December 31, 2014, the Company recorded $6.1 million as in-process research and development expense within the statement of operations, which represents the fair value of the license received from Caribou. The $6.1 million expense includes $4.1 million associated with the fair value of the Junior Preferred Units issued to Caribou and $2.0 million in committed cash payments under the services agreement, which were determined to be allocable to the value of the licenses received. The remaining $3.0 million in committed cash payments related to the services agreement are being recorded as research and development expense as the services are provided. For the period from May 7, 2014 (inception) through December 31, 2014 and for the year ended December 31, 2015, the Company recorded $0.3 million and $1.5 million, respectively, in research and development expense for services provided under the Caribou services agreement. The Company had prepaid research and development expenses recorded of $0.2 million and $0.4 million related to the services agreement as of December 31, 2014 and 2015, respectively.

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The Company accounted for the license from Caribou as an acquisition of in-process research and development assets and recorded the entire amount as in-process research and development expense as the Company did not acquire any employees, manufacturing or other facilities, developed processes or clinical stage assets as part of its agreement with Caribou.

*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 addition, in 2015, the Company entered into a two-year agreement to lease additional laboratory space and a one-year agreement to lease a corporate apartment.

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 $0.1 million during the period from May 7, 2014 (inception) to December 31, 2014 and $1.2 million during the year ended December 31, 2015.

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. The Company's contractual commitments under the committed first six years of this lease total $28.3 million. Payments under the contract are expected to begin in late 2016 when the Company is projected to gain access to the space.

The Company's contractual commitments under the Caribou agreements and property leases as of December 31, 2015 are as follows:

| Year Ending December 31, | Fixed Payments to Caribou | Property Leases | Total Commitments |
|---|---|---|---|
| | | (in thousands) | |
| 2016 | $ 1,500 | $ 945 | $ 2,445 |
| 2017 | — | 1,025 | 1,025 |
| 2018 | — | 843 | 843 |
| 2019 | — | 869 | 869 |
| 2020 | — | 73 | 73 |
| Thereafter | — | — | — |
| | $ 1,500 | $ 3,755 | $ 5,255 |

This table does not include (i) the property lease the Company entered into subsequent to December 31, 2015 or (ii) the Company's 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.

***Contingencies***

In connection with the July 2014 intellectual property license with Caribou, 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 United States patent application that is currently subject to interference proceedings declared by the Patent Trial and Appeal Board of the United States

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Patent and Trademark Office. If the Company's sublicensed patent family does not prevail in these proceedings, claims could be asserted against the Company during development or commercialization of a product that relies on this technology. Defense of any such claims would involve substantial litigation expense, and any successful claim of infringement against the Company could require the Company to pay substantial damages.

**7. Preferred Units and Preferred Stock**

The Company had issued Class A-2, Class A-1 and Junior preferred units (collectively, the "Preferred Units"), which converted to Series A-2, Series A-1 and Junior preferred stock upon the Reorganization. In August 2015, the Company issued Series B preferred stock (with the Series A-2, Series A-1 and Junior preferred stock, collectively referred to as the "Preferred Stock"). The Preferred Units were classified within members' equity.

In July 2014, the Company issued 2,857,142 Class A-1 Preferred Units at an issuance price of $1.05 for gross proceeds of $3.0 million, net of issuance costs of $0.2 million.

In July 2014, the Company issued 8,110,599 Junior Preferred Units with an aggregate fair value of $4.1 million in exchange for all of Caribou's membership interest in Intellia, LLC. Intellia, LLC was a holding company that was the original party to the license agreement with Caribou and otherwise had no other assets or operations prior to being merged with and into the Company in July 2014. Refer to Note 6, *Commitments and Contingencies*, for additional information regarding these licenses. The fair value per unit of the Junior Preferred Units as of the date of issuance was determined by the Company relying in part on the results of a third-party valuation prepared using the option-pricing method to determine the Company's enterprise value.

In September 2014, the Company issued an additional 5,714,287 Class A-1 Preferred Units at an issuance price of $1.05 per unit, for gross proceeds of $6.0 million, net of issuance costs of $0.2 million. Of these units, 4.8 million units were issued and sold to Novartis in contemplation of a future collaboration arrangement. These preferred units were subsequently determined to have a fair value of $1.51 per unit as of their date of issuance; therefore, a portion of the upfront consideration received under the collaboration arrangement was allocated to the carrying value of these preferred units when received during the year ended December 31, 2015. The fair value per unit of the Class A-1 Preferred Units as of the date of issuance was determined by the Company relying in part on the results of a third-party valuation prepared using the probability-weighted expected return method ("PWERM"), which used a combination of market approaches and an income approach to determine the Company's enterprise value.

In December 2014, the Company issued 2,666,666 Class A-2 Preferred Units to Novartis at an issuance price of $1.50 per unit for gross proceeds of $4.0 million, net of insignificant issuance costs, in contemplation of the collaboration and license arrangement entered into with Novartis at the same time. These preferred units were subsequently determined to have a fair value of $1.67 per unit as of their date of issuance; therefore, a portion of the upfront consideration received under the collaboration arrangement was allocated to the carrying value of these preferred units when received in 2015. The fair value per unit of the Class A-2 Preferred Units as of the date of issuance was determined by the Company relying in part on the results of a third-party valuation prepared using the PWERM, which used a combination of market approaches and an income approach to determine the Company's enterprise value.

In January 2015, the Company issued 1,333,333 Class A-2 Preferred Units at an issuance price of $1.50 per unit for gross proceeds of $2.0 million, net of insignificant issuance costs.

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Preferred Units consisted of the following as of December 31, 2014:

| | Preferred Units Issued and Outstanding | Carrying Value | Liquidation Preference |
|---|---|---|---|
| | | (in thousands) | |
| Class A-2 Preferred Units | 2,666,666 | $ 3,986 | $ 4,000 |
| Class A-1 Preferred Units | 8,571,429 | 8,407 | 9,000 |
| Junior Preferred Units | 8,110,599 | 4,055 | 8,516 |
| | 19,348,694 | $16,448 | $ 21,516 |

The Preferred Units had no conversion or redemption rights; therefore, the Company determined that these securities qualified for classification as permanent equity.

***Reorganization with Intellia Therapeutics, Inc.***

On August 20, 2015, the Company completed a series of transactions pursuant to which Intellia Therapeutics, LLC, the former sole stockholder and holding company parent, merged with and into Intellia Therapeutics, Inc., and Intellia Therapeutics, Inc. continued to exist as the surviving corporation. In connection with the Reorganization:

- holders of Intellia Therapeutics, LLC's outstanding Class A-2 Preferred Units received one share of Intellia Therapeutics, Inc. Series A-2 Preferred Stock for each Class A-2 Preferred Unit held immediately prior to the Reorganization, with an aggregate of 3,999,999 shares of Intellia Therapeutics, Inc. Series A-2 Preferred Stock issued in the Reorganization;
- holders of Intellia Therapeutics, LLC's outstanding Class A-1 Preferred Units received one share of Intellia Therapeutics, Inc. Series A-1 Preferred Stock for each Class A-1 Preferred Unit held immediately prior to the Reorganization, with an aggregate of 8,571,429 shares of Intellia Therapeutics, Inc. Series A-1 Preferred Stock issued in the Reorganization;
- holders of Intellia Therapeutics, LLC's outstanding Junior Preferred Units received one share of Intellia Therapeutics, Inc. Junior Preferred Stock for each Junior Preferred Unit held immediately prior to the Reorganization, with an aggregate of 8,110,599 shares of Intellia Therapeutics, Inc. Junior Preferred Stock issued in the Reorganization;
- holders of Intellia Therapeutics, LLC's outstanding Common Units received one share of Intellia Therapeutics, Inc. Founder Stock for each Common Unit held immediately prior to the Reorganization, with an aggregate of 2,298,000 shares of Intellia Therapeutics, Inc. Founder Stock issued in the Reorganization; and
- holders of Intellia Therapeutics, LLC's outstanding Incentive Units received restricted shares of Intellia Therapeutics, Inc. Common Stock in an amount equal in value to the value of such Incentive Units as determined by the applicable provisions of the Intellia Therapeutics, LLC operating agreement in effect immediately prior to the Reorganization, with an aggregate of 2,558,755 shares of Intellia Therapeutics, Inc. restricted common stock issued in the Reorganization.

In evaluating this transaction, the Company considered that (i) although the number of shares and ownership interests held by each stockholder changed nominally, the fair value of each stockholder's interest remained unchanged as a result of the Reorganization, and (ii) the Reorganization occurred between a parent and wholly-owned subsidiary, where the parent, Intellia Therapeutics, LLC, had no substantive operations. Based on this evaluation, 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's Series A-2 Preferred Stock, Series A-1 Preferred Stock, Junior Preferred Stock and Founder Stock are designated as Preferred Stock under its amended and restated certificate of incorporation. All outstanding shares of its Preferred Stock convert to shares of common stock on a one-for-0.6465903 basis.

The Preferred Stock issued in the Reorganization has the following rights and preferences:

***Conversion***—Prior to any automatic conversion of the Preferred Stock in connection with the closing of an initial public offering, each share of Preferred Stock is convertible at the option of the holder into the number of shares of common stock determined by dividing the respective "Original Issue Price" for such series of Preferred Stock by the applicable conversion price then in effect for such series of Preferred Stock. The conversion prices for each series of Preferred Stock are subject to adjustment in the event of certain dilutive issuances of common stock.

All shares of Preferred Stock are automatically convertible into common stock upon the earlier of (i) the closing of an underwritten public offering in which the public offering price is at least $13.3875 per share (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the common stock) and the net proceeds raised equal or exceed $60.0 million, (ii) in connection with any other underwritten public offering with the election of the holders of at least 67% of the outstanding shares of Preferred Stock, voting together as a single class on an as-converted to common stock basis, and (iii) the election of the holders of at least 67% of the outstanding shares of Preferred Stock, voting together as a single class on an as-converted to common stock basis, and the holders of at least a majority of the outstanding shares of Series B Preferred Stock, voting together as a single class on an as-converted to common stock basis.

***Voting Rights***—The holders of Preferred Stock are entitled to vote as a single class with the holders of common stock on all matters and are entitled to the number of votes equal to the number of whole shares of common stock into which the shares of the particular series of Preferred Stock are convertible. The holders of Series B Preferred Stock, voting together as a single class on an as-converted to common stock are entitled to elect one director to the Company's board of directors, the holders of Series A-1 Preferred Stock and Series A-2 Preferred Stock, voting together as a single class on an as-converted to common stock basis, are entitled to elect one director to the Company's board of directors, the holders of Junior Preferred Stock, voting together as a single class on an as-converted to common stock basis, are entitled to elect one director to the Company's board of directors and the holders of Preferred Stock and the holders of common stock, voting together as a single class on an as-converted to common stock basis, are entitled to elect the remaining directors.

***Dividends*** —The holders of Preferred Stock are entitled to receive non-cumulative dividends in preference to any dividends on common stock, in each case, only when and if declared by the Company's board of directors.

***Liquidation Preference***—In the event of any liquidation, dissolution or winding-up of the Company, including certain mergers or a disposition of all or substantially all of the assets of the Company (a "Deemed Liquidation Event") the Preferred Stock ranks senior to the Company's common stock and the holders of Preferred Stock shall be entitled to receive their original purchase price together with all accumulated but unpaid dividends prior to any distributions being made to common stock. Additionally, each class of Preferred Stock is successively more senior than the previous issued class of Preferred Stock, except for the Series A-1 Preferred Stock, which ranks *pari passu* with the Series A-2 Preferred Stock, and each holder of the more senior Preferred Stock shall be entitled to receive their original purchase price together with all accumulated but unpaid dividends prior to any distributions made to the less senior Preferred Stock. The order of seniority is Series B, Series A-2 and Series A-1, Junior Preferred and Founder Stock. Upon completion of the payment of the original purchase price and declared but unpaid dividends to the holders of Preferred Stocks, all of the remaining assets shall be distributed among the holders of Preferred Stock and common stock pro rata based on the number of shares of common stock held by each, assuming full conversion of all outstanding shares of Preferred Stock.

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The Preferred Stock has no redemption rights; however, because the holders of the Preferred Stock have the option to require redemption upon a Deemed Liquidation Event, which may be beyond the Company's control, the Preferred Stock has been classified as temporary equity. A Deemed Liquidation Event has not been deemed probable as of December 31, 2015.

***Issuance of Series B Preferred Stock***

In August 2015, the Company issued 13,336,601 shares of Series B Preferred Stock at an issuance price of $5.25 per share for gross proceeds of $70.0 million.

The rights and preferences of the Series B Preferred Stock are similar to those of the other series of Preferred Stock, except that, specifically, (1) the majority of the outstanding shares of Series B Preferred Stock, voting together as a single class on an as-converted to common stock basis, has the ability to control the election of the holders of Preferred Stock to convert to common, (2) the Series B preferred stockholders, voting together as a single class on an as-converted to common stock basis, are entitled to elect one director to the Company's board of directors, and (3) the Series B preferred stockholders are entitled to first preference in the event of a liquidation.

Preferred Stock consisted of the following as of December 31, 2015:

| | Preferred Shares Issued and Outstanding | Carrying Value | Liquidation Preference |
|---|---|---|---|
| | | (in thousands) | |
| Series B Preferred Stock | 13,336,601 | $67,263 | $ 70,017 |
| Series A-2 Preferred Stock | 3,999,999 | 6,249 | 6,000 |
| Series A-1 Preferred Stock | 8,571,429 | 9,750 | 9,000 |
| Junior Preferred Stock | 8,110,599 | 4,055 | 8,516 |
| Founder Stock | 2,298,000 | 1,240 | 2,413 |
| | 36,316,628 | $88,557 | $ 95,946 |

**8. Collaboration**

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

Under the terms of the collaboration, the Company and Novartis may research potential therapeutic, prophylactic and palliative applications of the CRISPR/Cas9 platform in HSCs and CAR T cells. Within the HSC therapeutic space, Novartis may obtain exclusive rights to a limited number of 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. 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 or commercialize at least one HSC product directed to at least one of their selected HSC targets.

The Company also agreed to collaborate with Novartis on research activities for CAR T cell targets under a research plan agreed upon by both parties. After completion of the research and development 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 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 their selected CAR T cell targets.

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In the last two years of the collaboration term, Novartis will have the option to select a limited number of targets for research, development and commercialization of *in vivo* therapies. Novartis is required to use commercially reasonable efforts to research, develop or commercialize at least one *in vivo* product directed to each of their selected targets. Novartis' *in vivo* target selections are subject to certain restrictions, including that the targets may not have been already reserved by the Company or be subject to another agreement.

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, 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 United States ("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. At date of issuance of the Class A-1 and A-2 Preferred Units in September and December 2014, the difference between the cash proceeds received from Novartis for the units and the $11.6 million estimated fair value of those units at date of issuance was determined to be $2.6 million.

The fixed portion of consideration under the collaboration arrangement was determined to be the $30.0 million of total technology access fees, for which there are no contingent terms. From that amount, the Company allocated $2.6 million to the preferred units purchased by Novartis to record those units based on their fair value at date of issuance. As a result, during the year ended December 31, 2015, the Company recorded an increase of $2.6 million to the carrying value its Class A-1 and A-2 Preferred Units and a corresponding decrease to the deferred revenue initially recorded in connection with the collaboration agreement with Novartis.

The significant deliverables of this multiple-element revenue arrangement were determined to be licenses CAR T cell and HSC targets and the associated research activities for these programs. The Company further determined that the licenses and associated research activities and joint steering committee participation did not have standalone value due to the specialized nature of the services to be provided by the Company. Therefore, the deliverables are not separable, and, accordingly, the license and services are treated as a single unit of accounting.

Net of the $2.6 million allocation, the fixed portion of consideration under the arrangement of $27.4 million is being recognized as collaboration revenue over the five-year performance period of the arrangement. As consideration for reimbursement of research and development activities is received, the Company is recognizing as collaboration revenue the portion of those payments representing the percentage of the performance period then completed. The remaining consideration is being recognized over the remaining portion of the five-year performance period on a straight-line basis. During the year ended December 31, 2015, the Company recorded revenue of $6.0 million related to the collaboration agreement with Novartis. As of December 31, 2015, deferred revenue under the Novartis arrangement was $10.3 million. There was no deferred revenue related to this arrangement as of December 31, 2014.

*Agreement Termination Rights*

The collaboration term ends in December 2019. The agreement ends (i) upon the expiration of Novartis' payment obligations; or (ii) on the date of expiration of the last-to-expire patent right that is licensed to the Company or Novartis. Novartis may terminate the agreement, without cause, upon 90 days' written notice to the

Company subject to certain conditions, including its payment of any accrued and future obligations as if the collaboration had continued through December 2019. Either party may terminate the agreement in the event of the other party's uncured material breach or insolvency.

**9. Equity-Based Compensation**

From inception through July 2015, the Company issued equity-based compensation awards in the form of common units or incentive units. In connection with the Reorganization, holders of the outstanding common units received one share of Intellia Therapeutics, Inc. Founder Stock, and holders of the outstanding incentive units received restricted shares of common stock of Intellia Therapeutics, Inc. There was no incremental compensation recognized from the conversion that occurred as a result of the Reorganization.

Each share of Founder Stock and each share of restricted common stock entitles the holder to one vote for each share of common stock into which each share is convertible on all matters submitted to a vote of the Company's stockholders. Founder stock and restricted stock holders are entitled to dividends when and if declared by the Board of Directors, subject to the preferential rights of other preferred stockholders.

These awards primarily vest as to 25% of the total units on the first anniversary of the vesting commencement date and then monthly, at the end of each subsequent month, over three years. The Company generally grants equity-based awards with service conditions only. As of December 31, 2015, the Company had reserved 1,128,717 shares for future grant. In February 2016, the Company increased the number of shares reserved for future grant by 1,529,411 shares.

***Equity-Based Compensation***

The Company recorded equity-based compensation expense in its consolidated statements of operations as follows:

| | Period from May 7, 2014 (inception) to December 31, 2014 | Year Ended December 31, 2015 |
|---|---|---|
| | (in thousands) | |
| Research and development | $ 83 | $ 1,061 |
| General and administrative | 225 | 247 |
| | $ 308 | $ 1,308 |

***Founder Stock and Restricted Stock***

Compensatory common and incentive units, and the corresponding Founder Stock and restricted stock issued in replacement of common and incentive units in the Reorganization, are valued at the fair value of the underlying security. 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.

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The following table summarizes the Company's compensatory Founder Stock (common unit) activity since inception:

| | Number of Shares | Weighted Average Grant Date Fair Value per Share |
|---|---|---|
| Unvested common units as of January 1, 2015 | 1,013,821 | $ 0.37 |
| Vested | (577,312) | $ (0.37) |
| Unvested Founder Stock as of December 31, 2015 | 436,509 | $ 0.37 |

The following table summarizes the Company's compensatory restricted stock (incentive unit) activity since inception:

| | Number of Shares | Weighted Average Grant Date Fair Value per Share |
|---|---|---|
| Unvested incentive units as of January 1, 2015 | 1,558,498 | $ 0.35 |
| Issued | 877,456 | $ 1.34 |
| Effect of Reorganization | 154,606 | $ — |
| Vested | (613,719) | $ (0.36) |
| Forfeited | (31,805) | $ (1.34) |
| Unvested restricted stock as of December 31, 2015 | 1,945,036 | $ 0.78 |

The aggregate intrinsic value of Founder Stock awards that vested during each of the periods from May 7, 2014 (inception) to December 31, 2014 and the year ended December 31, 2015 was $0.1 million and $2.2 million, respectively. The aggregate intrinsic value of restricted stock awards that vested during the year ended December 31, 2015 was $3.3 million.

As of December 31, 2015, there was $3.5 million of unrecognized equity-based compensation related to Founder Stock and restricted stock that is expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 3.0 years.

***Stock Options***

The Company uses the Black-Scholes option-pricing model to measure the fair value of stock option awards. Key assumptions used in this pricing model on the date of grant for options granted to employees are as follows:

| | Year Ended December 31, 2015 |
|---|---|
| Risk-free interest rate | 1.5% |
| Expected life of options | 6.0 years |
| Expected volatility of underlying stock | 82.6% |
| Expected dividend yield | 0.0% |

There were no stock option awards granted in 2014.

The risk-free interest rate is based upon the U.S. Treasury yield curve in effect at the time of grant, with a term that approximates the expected life of the option. The Company calculates the expected life of options granted to employees using the simplified method as the Company has insufficient historical information to provide a basis for estimate. The Company determines the expected volatility based on the historical volatility of

a peer group of comparable publicly traded companies with product candidates in similar stages of development to the Company's product candidates. The Company has applied an expected dividend yield of 0.0% as the Company has not historically declared a dividend and does not anticipate declaring a dividend during the expected life of the options.

The following table summarizes the Company's stock option activity from inception through December 31, 2015:

| | 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, 2014 | — | $ — | | |
| Granted | 456,374 | 6.04 | | |
| Outstanding at December 31, 2015 | 456,374 | $ 6.04 | 9.8 | $ 166 |
| Exercisable at December 31, 2015 | — | $ — | — | $ — |

The weighted average grant date fair value of these awards was $4.24 per share.

As of December 31, 2015, there was $1.8 million of unrecognized stock-based compensation related to stock options that are expected to vest. The Company expects to recognize this expense over a weighted-average period of 3.7 years.

In February 2016, the Company granted 2,161,558 stock options at an exercise price per share of $6.83.

**10. Loss per Unit**

Basic and diluted loss per common unit and per incentive unit were calculated as follows:

| | Period from May 7, 2014 (inception) to December 31, 2014 (in thousands, except per unit data) |
|---|---|
| Net loss | $ (9,539) |
| Weighted average common units outstanding, basic and diluted | 826 |
| Net loss per common unit, basic and diluted | $ (11.55) |

The Company's Preferred Stock has the right to participate in earnings and distributions of the Company but are not obligated to share in losses. As a result, in periods of net loss, the Company allocated losses on a pro rata basis to the holders of its Common Units and Incentive Units.

Following the Reorganization, the Company calculates loss per share attributable to common stockholders based on its outstanding common stock.

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

| | Year Ended December 31, 2015 (in thousands, except per share data) |
|---|---|
| Net loss | $ (12,397) |
| Weighted average shares outstanding, basic and diluted | 243 |
| Loss per share attributable to common stockholders, basic and diluted | $ (51.02) |

The following common stock equivalents have been excluded from the calculations of diluted loss per unit or share because their inclusion would have been antidilutive.

| | Period from May 7, 2014 (inception) to December 31, 2014 | Year Ended December 31, 2015 |
|---|---|---|
| | (in thousands) | |
| Preferred units | 11,382 | — |
| Convertible preferred stock | — | 21,363 |
| Unvested common units | 596 | — |
| Unvested incentive units | 1,558 | — |
| Unvested restricted stock | — | 1,945 |
| Stock options | — | 456 |
| | 13,536 | 23,764 |

***Unaudited Pro Forma Loss per Share***

Pro forma net loss per share is calculated as follows:

| | Period from May 7, 2014 (inception) to December 31, 2014 | Year Ended December 31, 2015 |
|---|---|---|
| | (in thousands, except per unit and per share data) (unaudited) | |
| Net loss | $ (9,539) | $ (12,397) |
| Weighted average common units outstanding, basic and diluted | 826 | — |
| Weighted average shares outstanding, basic and diluted | — | 243 |
| Pro forma adjustment for conversion of all units in the Reorganization and the subsequent assumed automatic conversion of all preferred stock into shares of common stock upon the closing of the proposed initial public offering | 5,991 | 17,421 |
| Pro forma weighted average shares outstanding, basic and diluted | 6,817 | 17,664 |
| Pro forma net loss per share, basic and diluted | $ (1.40) | $ (0.70) |

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**11. Related Party Transactions**

In July 2014, the Company issued Caribou 8,110,599 Junior Preferred Units. As a result of this and related transactions, Caribou owned 33.7% and 20.2% of the Company's fully diluted equity as of December 31, 2014 and December 31, 2015, respectively. Refer to Note 6, *Commitments and Contingencies*, for additional information regarding these agreements.

During the period from May 7, 2014 (inception) to December 31, 2014, the Company recognized $6.1 million in in-process research and development expense and $0.2 million in research and development expense and, as of December 31, 2014, had recorded current and non-current obligations of $1.7 million related to the license and service agreements with Caribou. 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. In addition, the Company recognized $0.2 million and $1.1 million in general and administrative expense during the period from May 7, 2014 (inception) to December 31, 2014 and the year ended December 31, 2015, respectively, related to the Company's obligation to pay 30.0% of Caribou's patent prosecution, filing, and maintenance costs under the intellectual property license agreement with Caribou.

In connection with its entry into a 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. As a result of these transactions, Novartis owned 28.9% of the Company's fully diluted equity as of December 31, 2014. In August 2015, Novartis acquired 761,905 shares of the Company's Series B Preferred Stock. As a result of this transaction, Novartis collectively owned 19.2% of the Company's fully diluted equity as of December 31, 2015. Refer to Note 8, *Collaboration*, for additional information regarding this collaboration agreement.

During the year ended December 31, 2015, the Company recognized $6.0 million in collaboration revenue related to this collaboration. As of December 31, 2015, the Company had recorded accounts receivable of $1.0 million and deferred revenue of $10.3 million related to this collaboration.

From May 7, 2014 (inception) to September 2014, the Company received consulting and management services from Atlas Venture Advisors, Inc., which through its affiliate, Atlas, owned 18.5% of the Company's fully diluted equity as of December 31, 2014. The Company paid Atlas Venture Advisors, Inc. $0.3 million for these services, including reimbursement of expenses, in the period from May 7, 2014 (inception) to December 31, 2014. No such services were provided in 2015.


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