

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

**FORM 10-K**

(Mark One)

- ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
For the fiscal year ended December 31, 2016
- TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission File Number 001-37687

**EDITAS MEDICINE, INC.**  
(Exact name of registrant as specified in its charter)

Delaware  
(State or other jurisdiction of  
incorporation or organization)

11 Hurley Street  
Cambridge, Massachusetts  
(Address of principal executive offices)

46-4097528  
(I.R.S. Employer  
Identification No.)

02141  
(Zip Code)

(617) 401-9000  
(Registrant's telephone number, including area code)

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

Title of each class  
Common Stock, \$0.0001 par value per share

Name of each exchange on which registered  
NASDAQ Global Select Market

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

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

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

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

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

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

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

Large accelerated filer  Non-accelerated filer  Accelerated filer  Smaller reporting company   
(Do not check if a smaller reporting company)

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

As of June 30, 2016, the last day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's Common Stock held by non-affiliates of the registrant was approximately \$442,566,248, based upon the closing price of the registrant's Common Stock on June 30, 2016.

The number of shares of the registrant's Common Stock outstanding as of February 1, 2017 was 36,679,926.

**Editas Medicine, Inc.**  
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**References to Editas**

Throughout this Annual Report on Form 10-K, the “Company,” “Editas,” “Editas Medicine,” “we,” “us,” and “our,” except where the context requires otherwise, refer to Editas Medicine, Inc. and its consolidated subsidiary, and “our board of directors” refers to the board of directors of Editas Medicine, Inc.

**Special Note Regarding Forward-Looking Statements and Industry Data**

This Annual Report on Form 10-K contains forward-looking statements regarding, among other things, our future discovery and development efforts, our future operating results and financial position, our business strategy, and other objectives for our operations. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. There are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by forward-looking statements. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the section entitled “Risk Factors” in Part I that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

This Annual Report on Form 10-K includes statistical and other industry and market data, which we obtained from our own internal estimates and research, as well as from industry and general publications and research, surveys, and studies conducted by third parties. Industry publications, studies, and surveys generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe that each of these studies and publications is reliable, we have not independently verified market and industry data from third-party sources. While we believe our internal company research is reliable and the market definitions are appropriate, neither such research nor these definitions have been verified by any independent source.

## PART I

### Item 1. Business

We are a leading genome editing company dedicated to treating patients with genetically defined diseases by correcting their disease-causing genes. We believe that we have entered a new era of genomic medicine as the growth of genomic information in recent decades has significantly expanded the understanding of genetically defined diseases. A new technology known as CRISPR (clustered, regularly interspaced short palindromic repeats) has the potential to achieve precise, directed changes in DNA. The confluence of these two streams of scientific endeavor, understanding genetic defects and having the tools to be able to address them, creates the opportunity for us to achieve a longstanding goal of medicine: to treat the root causes of diseases at the genetic level. Our mission is to translate the promise of our science into a broad class of transformative genomic medicines to benefit the greatest number of patients.

We are developing a proprietary genome editing platform based on CRISPR technology. CRISPR uses a protein-RNA complex composed of an enzyme, including either Cas9 (CRISPR associated protein 9) or Cpf1 (CRISPR from *Prevotella* and *Francisella* 1), bound to a guide RNA molecule designed to recognize a particular DNA sequence. Once the complex binds to the DNA sequence it was designed to recognize, the complex makes a specific cut in the DNA, ultimately triggering the cell's DNA repair machinery to change the targeted sequence. Our platform consists of four interrelated components: nuclease engineering, delivery, control and specificity, and directed editing. These components are designed to develop medicines that specifically address a wide variety of genetic targets, reach the site of disease safely and effectively, tightly and specifically control the editing process, and drive the right kind of genetic repair. Our preclinical drug discovery platform uses the flexibility of CRISPR technology to enable rapid reprogramming of the guide RNA complex with the potential to direct it to almost any site in the human genome. Using this platform, we aim to develop and advance a broad range of therapies for genetically defined diseases.

The Cpf1 enzyme complements the Cas9 enzyme as the Cpf1 enzyme is structurally distinct, has independent intellectual property, and has several potential benefits, including:

- increasing the number of sites in the genome that can be edited, because it has distinct protospacer adjacent motifs;
- simpler manufacturing and delivery, because the system requires only a short, single CRISPR guide RNA; and
- increased efficiency and accuracy for some forms of gene repair, because it makes staggered DNA cuts.

Our product development strategy is to target genetically defined diseases with an initial focus on debilitating illnesses where there are no approved treatments and where the genetic basis of disease is well understood. Over time, we also intend to develop medicines that may address genetically treatable diseases in addition to genetically defined diseases. A genetically defined disease may be treated by correcting a disease-causing gene, whereas a genetically treatable disease is a disease that does not necessarily have a single, disease-causing gene, but which nonetheless may be treated by editing genes to ameliorate or eliminate the signs or symptoms of that disease. We are advancing over a dozen discovery research programs that we have selected based on our assessment of the structure of the genetic mutation and edit required, our ability to deliver the product candidate to the site of disease, the severity of the disease, the ability to identify appropriate patients, and the availability of informative preclinical assays and models and suitable clinical endpoints. Our most advanced research program is designed to address Leber Congenital Amaurosis type 10, or LCA10, a specific genetic form of vision loss that leads to blindness in childhood and has no available therapies or potential treatments in clinical trials in either the United States or European Union, or EU. The localization of LCA10 disease in the eye allows us to efficiently apply our technology in a context that is confined and relatively uncomplicated compared to many of the systemic illnesses we also anticipate treating over time. We aim to initiate a clinical natural history study in mid-2017 to evaluate the clinical course and characteristics of LCA10 more extensively, and we aim to file an investigational new drug, or IND, application by the end of 2017 for our LCA10 program. We believe achievement of proof-of-concept in a disease of the eye has the potential to validate our platform technology, including its potential

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application to other organs and diseases. Our additional research programs address genetic, infectious, and oncologic diseases of the liver, lung, blood, eye, and muscle.

We believe our genome editing technologies have the potential to improve the characteristics of cellular therapies, including engineered T cells to treat cancer. To realize this potential, in May 2015, we entered into a collaboration with Juno Therapeutics, Inc., or Juno Therapeutics, a leader in the emerging field of immuno-oncology. Under the collaboration, we received an upfront payment of \$25.0 million, a milestone payment of \$2.5 million related to technical progress in a research program under the collaboration, and have the potential to receive approximately \$700 million in aggregate in potential research, regulatory, and commercial sales milestone payments for the first products developed in the three research programs established in the collaboration. In addition, we are eligible to receive research support of up to \$22.0 million over a five year term and across the three programs under the collaboration, subject to adjustment in accordance with the terms of the collaboration, of which we had recognized \$4.8 million as of December 31, 2016. By working with Juno Therapeutics, we hope that together we will be able to discover and develop the next generation of engineered T cell therapies that have the potential to substantially advance the field of cancer immunotherapy. We believe this collaboration exemplifies our strategy of selectively establishing alliances with leaders in their fields to realize the full therapeutic potential of genome editing.

Our company was founded by world leaders in genome editing, who are affiliated with institutions that include The Broad Institute Inc., or Broad, of the Massachusetts Institute of Technology, or MIT, and Harvard University, President and Fellows of Harvard College, or Harvard, MIT, and The General Hospital Corporation d/b/a Massachusetts General Hospital, or MGH. Through their service as consultants and advisors, our founders were instrumental in defining the initial scientific vision for our company. Collectively, our founders have made many fundamental discoveries in the field of genome editing and have enabled the translation of CRISPR from its origins in bacterial systems to its application in mammalian cells. Among our founders, Drs. Feng Zhang, George Church, David Liu, and J. Keith Joung continue to provide important scientific guidance and insights to us through ongoing consulting and advisory arrangements. Their discoveries, along with inventions by scientists at our company, have led to our broad portfolio of intellectual property, including the patent estates licensed from those founders' institutions. In connection with their consulting and advisory arrangements with us, Drs. Zhang, Church, Liu, and Joung have assignment of inventions obligations to us with respect to the services they perform for us, subject to limitations, including that such assignment obligations do not extend to their work in other fields or to the intellectual property arising from their employment with their respective academic and research institutions. As of December 31, 2016, our portfolio included 41 issued U.S. and European patents and over 500 pending patent applications. We believe the breadth and depth of our patent estate is a substantial asset and has the potential to provide us with a durable competitive position in the marketplace.

We believe that our team and our culture are critical to our success. The lifeblood of our company is exceptional scientists and company-builders with experience across leading biopharmaceutical companies and academic research laboratories. Our company is distinguished by our leaders' substantial experience in translating groundbreaking scientific platforms into therapeutic products and product candidates at Adnexus Therapeutics, Alnylam Pharmaceuticals, Avila Therapeutics, Bristol-Myers Squibb, Millennium Pharmaceuticals, Novartis, and Sanofi Genzyme. In addition, our board of directors has deep experience in guiding biotechnology companies through rapid growth and the development of complex, breakthrough science.

Every decade over the past 40 years, an important class of medicines has emerged, such as recombinant proteins, monoclonal antibodies, and RNA-based drugs. These new categories of medicines have brought forth important therapies for previously untreated diseases. In our view, genome editing with CRISPR has the potential to be one of the next major new categories. At Editas Medicine, we believe we can make that potential a reality.

### **Our Values**

Our values are a critical foundation upon which we build this organization. These values are:

- **Community: One Team—Many Voices—Shared Mission**

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- **Resilience:** Respect—Grow—Learn
- **Ingenuity:** Be Bold—Answer Unknowns—Create Therapies
- **Science:** Impeccable—Rigorous—Meaningful
- **Passion:** Love It—Do It—Own It
- **Revolution:** Discover—Translate—Cure

## **Our Strategy**

We aim to transform the treatment of a broad range of genetically defined diseases by building an integrated genomic medicine company focused on creating a novel class of therapeutics to meet patients' needs. Key elements of our strategy are to:

- **Build the preeminent genomic medicine company.** Developing a major new technology like CRISPR requires an exceptional organization. We have assembled a group of world leaders in the fields of genome editing, gene therapy, nucleic acid pharmaceuticals, and orphan diseases. We will continue to build and expand our team to encompass all the capabilities needed to develop and commercialize medicines and to run an outstanding company.
- **Advance therapeutic programs rapidly and rigorously to address patients' needs.** Our strategy centers around developing medicines where the genetic basis of disease is well understood and where we believe our approach can provide unique benefits by addressing the root cause of the disease. For example, we chose LCA10 as our first program due to the absence of therapeutic options and the amenability of the underlying mutation to genome editing. We believe our product development strategy will initially result in therapies for rare and orphan diseases that have the potential to advance rapidly and deliver substantial benefits for patients, and we aim to identify and advance product candidates into clinical trials on a consistent basis.
- **Perfect the tools to repair any broken gene.** Our genome editing platform is composed of a broad set of tools that we use to design and optimize product candidates for many different genetically defined diseases. We plan to continue to invest resources as we further expand the four interrelated components of our platform: nuclease engineering, delivery, control and specificity, and directed editing. We are developing new capabilities in each of these components so that we can fully realize the therapeutic potential of genome editing.
- **Accelerate the science of genome editing.** Our founders and scientists are leaders in the extremely fast-moving field of genome editing. We are committed to maintaining and extending our leadership in this field while empowering the broader scientific field through continued internal and external investment in basic science and translational research in genome editing.
- **Collaborate to realize the full potential of genome editing to create medicines.** Because of the broad potential for our technology, we have and will continue to seek collaborations with pioneering companies, such as Juno Therapeutics, and with leading academic and research institutions to expand and improve the range of product candidates we discover and develop.
- **Commercialize products to bring new medicines to patients.** We believe that therapies for genetically defined diseases can often be brought to patients through a small, targeted commercial organization without the need for a commercial partner. In these cases, we intend to commercialize our own products to retain the greatest value for shareholders. For any other products, we intend to maximize the commercial opportunity through selective partnering.

## **Our Focus—Genome Editing**

Humans possess a genome sequence of roughly three billion base pairs of nucleotides, the building blocks of the DNA double helix. DNA serves as the road map for cellular function. Small changes, or mutations, routinely occur in the base pairs of our DNA. At the molecular level, these mutations can be categorized as single base pair changes, small insertions or deletions, large deletions, duplications, or repetitive sequence expansions. A mutation could occur on one or both alleles, or copies, of a gene in a cell. In some cases, these mutations can lead to a failure to produce proteins that are necessary for normal function or the production of abnormal proteins, either of which can cause disease. Abnormal proteins can interfere with the function of the normal protein or lead to a new deleterious effect called a toxic gain of function. Genetically defined diseases vary dramatically in their pathologies, their sites of manifestation, and the specific natures of their root causes. Currently, there are approximately 6,000 diseases that are known to be caused by genetic mutations. Familiar examples of genetically defined diseases include cystic fibrosis, Duchenne muscular dystrophy, Huntington’s disease, retinitis pigmentosa, and sickle cell anemia.

Major investments in the human genome project, clinical sample collection and characterization, and the subsequent development of low cost and rapid DNA sequencing and informatics tools have revolutionized the understanding of genetically defined diseases and paved the way for advancing the field of genomic medicine. For example, many diseases previously thought to be genetically complex in nature have now been re-categorized as several distinct diseases that present with similar clinical dispositions, but are caused by different single-gene defects. Diseases caused by single-gene defects are known as monogenic disorders. The identification of monogenic disorders has resulted in a shift towards therapeutic approaches targeted at specific mutations, as opposed to the symptom-specific or pathology-specific approaches of the past. We believe monogenic disorders are particularly suitable for treatment by genome editing because a single edit has the potential to correct the disease.

While genetic defects are now recognized as the causes of many diseases, the vast majority of these diseases lack effective treatments. Of the estimated 6,000 diseases that are known to be caused by genetic mutations, we believe fewer than 5% are served by approved therapies. In some cases, these existing therapies only treat the symptoms of the disease. In other cases, existing therapies modify the course of disease, but do not address the underlying genetic defect.

### *The Field of Genomic Medicine*

Genomic medicine harnesses the knowledge of genetics to guide the care of patients and create new therapies. There are several technologies that have the potential to create medicines in this field. These technologies can be grouped into two broad categories: gene augmentation and genome editing. Each approach seeks to address genetically defined diseases at the level of DNA. However, gene augmentation, which is commonly called gene therapy, and genome editing differ fundamentally with regard to the kind of genomic change they seek to accomplish.

Gene therapy is an approach whereby a new gene is transferred into cells to augment a defective gene. This can either be through insertion of the new gene directly into a patient’s DNA without specific regard to the site of insertion or delivering a piece of DNA to exist alongside the patient’s genome without being integrated into it. Gene therapy transfers new DNA into cells, however it does not remove or modify the defective DNA and it generally introduces the new genetic material in a location where it is not subject to the cell’s normal control and feedback mechanisms. This approach is suited for a finite set of genetically defined diseases.

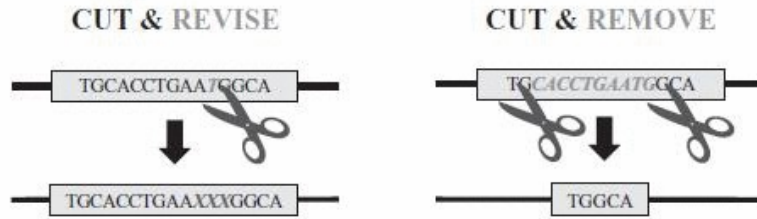
Genome editing is the process of revising, removing, or repairing defective DNA *in situ*. Genome editing corrects the defective DNA in its native location, and consequently the repaired genetic region retains the cell’s normal control and feedback mechanisms. The diversity of genetic drivers of disease demands a variety of solutions. Genome editing has the potential to deliver a variety of types of genome modification to address a broad range of genetically defined diseases.

At its core, genome editing is a two-step process. In the first step, an enzyme is brought to the desired site and makes a specific cut. This enzyme, which is called a DNA endonuclease, is capable of cutting one or both strands in the double-stranded DNA. After the desired cut or cuts are made, the cell’s DNA repair machinery responds to complete the edit through one of two possible mechanisms—non-homologous end joining or homology directed repair—that can be

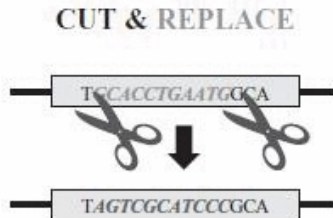
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harnessed for therapeutic effect in a range of ways. These types of edits could be applied to one or both alleles of the gene in the cell depending on the nature of the mutation.

The first mechanism, non-homologous end joining, or NHEJ, occurs in the absence of a DNA template for the cell to copy as it repairs a DNA cut. The NHEJ response tends to leave small insertions and deletions at the cut site, collectively referred to as indels. The NHEJ mechanism can be used to either cut and revise the targeted gene or to cut and remove a segment of DNA, depending on how many cuts are made. In the “cut and revise” process, depicted on the left below, a single cut is made, which can result in the creation of an indel during the repair process. In the “cut and remove” process, depicted on the right below, two cuts are made, which results in the removal of the intervening segment and the joining of the two ends of DNA. This approach could be used to delete either a small or a large segment of DNA depending on the type of repair desired.



The second mechanism, homology directed repair, or HDR, occurs in the presence of a DNA template that is similar to the DNA that has been cut. The cell can use the template to construct reparative DNA, resulting in the replacement of defective genetic sequences with correct ones. This can be thought of as a “cut and replace” process. As shown in the example below, HDR is used to replace a defective sequence of GCACCTGAATG with the correct sequence of AGTCGCATCCC.



Whether NHEJ or HDR is likely to be more therapeutically effective depends on the nature of the targeted genetic defect. The ability of genome editing approaches to utilize both mechanisms provides the opportunity to develop therapies for larger patient populations and a broader range of indications than either of the individual mechanisms alone. Although many of our initial programs utilize the NHEJ mechanism, we believe that the combination of our investment in the science of HDR and the work we and others are doing to modulate how cells use different repair pathways has the potential to result in medicines that take advantage of either mechanism to arrive at the desired genomic correction.

### *Advantages of CRISPR for Genome Editing*

CRISPR technology uses a protein-RNA complex composed of a type of enzyme, referred to as an endonuclease, bound to a guide RNA molecule that has been designed to recognize a particular DNA sequence. This recognition occurs when the appropriate portion of the guide RNA matches a DNA sequence, and when that DNA sequence is next to a short DNA sequence called the protospacer adjacent motif, or PAM. A PAM is part of the overall



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DNA pattern sought by the guide RNA complex to recognize a location in the genome. We believe that CRISPR technology has three principal advantages for genome editing:

- *Rapid, comprehensive, and systematic identification of product candidates.* The key targeting mechanism for the endonuclease, whether it is Cas9 or Cpf1, is an engineered guide RNA, which can be rapidly replaced with a different guide RNA or optimized by changes as small as a single nucleotide. This allows for the flexible design, synthesis, and testing of hundreds of guide RNA/endonuclease combinations for each genetic target in order to find those that cut the DNA target with the optimal efficiency and specificity. In contrast, other commonly used DNA nucleases for genome editing have inherently limited flexibility. For example, zinc finger nucleases, engineered meganucleases, and transcription activator-like effector nucleases, or TALENs, use proteins for DNA sequence recognition to bring the endonuclease to the site of the genome where cleavage is desired, requiring the creation of an entirely new protein for each target site.
- *Simultaneous and efficient targeting of multiple sites.* In CRISPR technology, multiple guide RNAs can be provided, enabling the simultaneous and efficient targeting of multiple sites. This ability to target multiple DNA sequences expands the applicability of CRISPR technology and also creates the potential for self-regulating systems that improve on the specificity of genome editing. To address more than one target, other genome editing technologies require the engineering, characterization, manufacture, and delivery of distinct nuclease proteins for each target.
- *Availability of different types of edits.* The availability of the different engineered variants of Cas9 allows for different types of cuts for genome editing, including cuts of both strands of the DNA or either the top or the bottom strand only. In the most broadly exploited genome editing CRISPR systems, the protein endonuclease is a single protein, the Cas9 enzyme, which contains two independent endonuclease sites each responsible for cutting one of the two DNA strands. Importantly, either or both of these sites can be rendered inactive by making specific changes to the Cas9 protein. When one site is rendered inactive, the resulting protein makes either one cut on the top or bottom strand, which is referred to as a nick. This may be a critical component of improved HDR-driven approaches because the type of DNA cut can influence the type of repair mechanism used by a cell in response to that cut. We believe the ability to modify CRISPR technology to allow for different types of cuts will expand the potential of our genome editing platform.

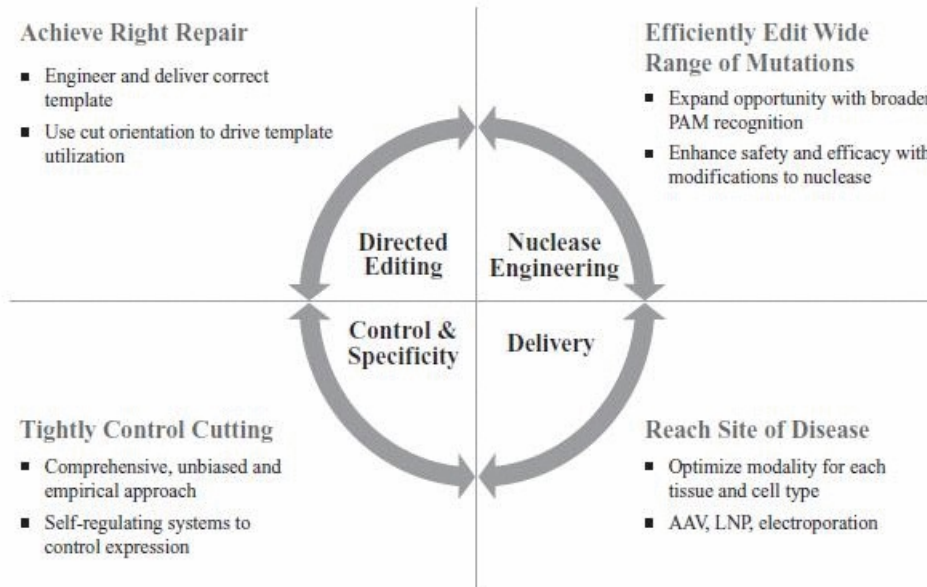
### **Advantages of Our Genome Editing Platform**

In order to fully realize the broad potential of CRISPR technology in developing genome editing medicines, we believe we must achieve each of the following four goals:

- specifically edit a wide range of mutations at different genomic locations,
- reach the site of disease,
- tightly control the cutting, and
- achieve the right repair.

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We are developing a proprietary genome editing platform consisting of four interrelated components that are designed to meet these goals. Each component is underpinned by several specific technologies and capabilities. With our platform we are able to design and optimize each element of the product configuration necessary to achieve the desired edit, including the Cas9 or Cpf1 variant, the sequence and structure of the guide RNA(s), the delivery vector, and elements to control expression in cells or to drive the desired repair mechanism.



- **Nuclease Engineering:** We use our genome editing platform to identify and optimize both the enzyme, including both Cas9 and Cpf1, as well as advanced forms of each, and the guide RNA molecule, to create what we believe will be the optimal endonuclease-guide RNA complex for a given disease target. We have made substantial advances in the characterization and modification of different natural and engineered variants of Cas9 and Cpf1 enzymes and in the design, synthesis, modification, analysis, and characterization of guide RNAs. We believe the diversity of the Cas9 and Cpf1 enzymes that we are currently employing and those that we are continuing to further develop have the potential to provide us with a competitive advantage as we develop a range of products with different technical needs. We believe our systematic approach to measurement of both the efficiency and specificity of multiple possible enzyme and guide RNA combinations enables us to optimize the identification of lead molecules to progress into more advanced testing. Our aim is to continue to develop new engineered Cas9 and Cpf1 enzymes with altered PAM specificities, different DNA cutting capabilities, and additional advanced properties. The range of natural and engineered variants of Cas9 and Cpf1 have significantly expanded the number of sites in the human genome that we can potentially target. As compared to the most commonly used, naturally-occurring version of Cas9, from the bacterial species *S. pyogenes*, the range of endonucleases in our platform can target approximately ten times as many genomic sites. We believe that further developing our nuclease engineering capabilities will allow us to further broaden the range of diseases we can treat while at the same time ensuring that our products have the best possible safety profiles.
- **Delivery:** An appropriate product configuration must be designed and optimized to provide efficient and tightly controlled delivery to the desired tissue or cell type. Our strategy is to leverage existing delivery technologies to target cell types of interest while developing next generation capabilities as warranted. We are currently exploring, and will continue to explore, a variety of delivery approaches, including

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adeno-associated viruses, or AAVs, lipid nanoparticles, or LNPs, and the use of electroporation. In addition, there are three types of molecules that we can deliver to a cell to effect genome editing: DNA, RNA, or a ribonucleoprotein, or RNP. Our genome editing platform includes multiple, modular delivery modes that can be efficiently adapted to deliver different CRISPR genome editing components to address the specific needs of each disease targeted.

- *Control and Specificity:* Control of cellular exposure to the endonuclease-guide RNA complex and specificity of the DNA cut are important to optimizing the location and duration of editing activity. We believe these features are critical to designing medicines that are both safe and effective, and we are developing and applying technologies in both areas. We have implemented multiple, discrete analytical methods that provide comprehensive and unbiased assessments of specificity to minimize off-target effects. To optimize the specificity of any product candidate we may develop, there are a number of different aspects of the product configuration that we will refine in addition to the sequence of the guide RNA. The length of the guide RNA, the type of Cas9 or Cpf1 enzyme, the delivery vector, the use of tissue-selective promoters, and the duration of exposure all contribute to overall specificity, and we seek to optimize each of these elements for every program. In addition, to reduce the persistence of genome editing activity, we are developing self-regulating genome editing systems designed to deliver not only the endonuclease guide RNA complex, but also an “off switch” that reduces the presence of the endonuclease guide RNA complex over time.
- *Directed Editing:* There are different mechanisms that a cell can use to repair cuts in DNA. Each mechanism results in different kinds of genetic changes. We are developing approaches to selectively harness specific DNA repair mechanisms to be able to drive the appropriate type of repair for a given disease. The ability to direct the DNA repair mechanism and influence the utilization of a DNA repair template is critical to achieving the broadest potential for our platform. We believe that our ability to understand and direct the repair mechanisms used by cells creates opportunities to improve our existing programs and opens up new opportunities to develop medicines, including medicines that rely on specific template utilization events.

All of our research programs have emerged from our proprietary genome editing platform.

### **Our Product Development Criteria**

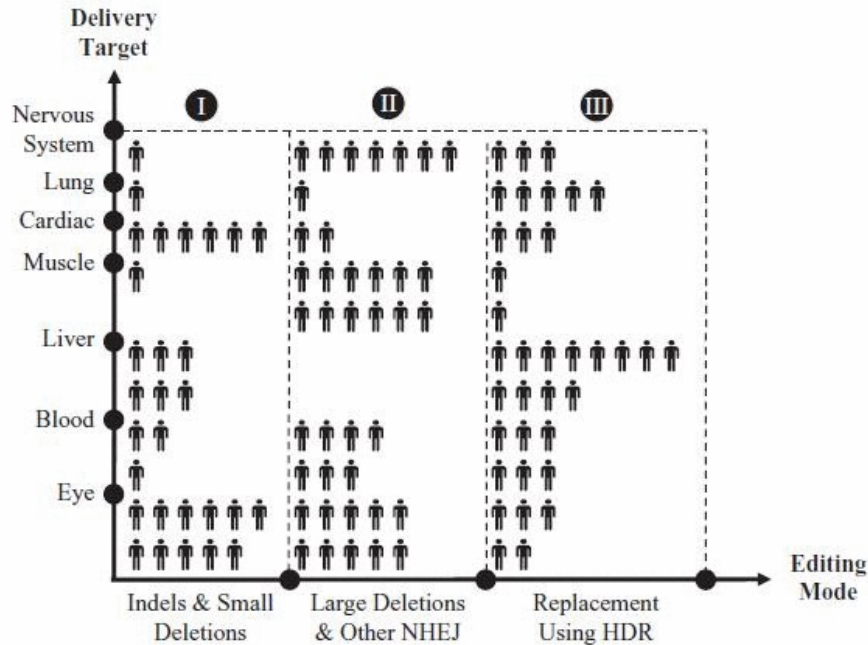
We are targeting genetically defined diseases with a focus on debilitating illnesses where there are unmet medical needs and where the genetic basis of the disease is well understood. Our comprehensive project evaluation and selection process takes into consideration the following criteria:

- *Medical need*—lack of or inadequate approved therapies and disease severity;
- *Opportunity for genome editing*—other therapeutic approaches unlikely to be helpful;
- *Nature of genetic mutation*—whether the mutation is accessible and can be feasibly corrected;
- *Delivery modality*—whether the delivery modality has been shown to be safe in patients;
- *Pathophysiology of the disease and treatment window*—presence of viable cells that can be edited as the disease progresses and potential for treatment through genome editing;
- *Safety and therapeutic index*—ability to assess, monitor, and/or minimize safety risks given the biology of the disease and the anticipated delivery system;
- *Clinical development path*—consideration of factors such as availability of patients, speed of disease progression, presence of predictive biomarkers, and robust and measurable clinical endpoints;

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- *Regulatory path*—existence of safety and tolerability models as well as suitable clinical endpoints; and
- *Commercial opportunity*—assessment of potential market, including patient population, competitive landscape, and reimbursement.

We believe our systematic approach to developing medicines based on CRISPR technology provides opportunities across a range of different genetically defined diseases. We aim to develop and commercialize biologic medicines for patients with these types of diseases. Where appropriate or necessary, we may do so in collaboration with strategic partners. If successful, we believe our research programs have the potential to yield therapies comprising a combination of elements that may include protein, DNA, and RNA components, which are collectively often referred to as biologics, and which differ from traditional small molecule pharmaceuticals in their greater complexity of manufacturing and delivery. As shown below, as we expand the technical capabilities of our platform, the number of potential patients and range of diseases that can potentially be addressed will grow. Our first programs to develop genome editing medicines take advantage of the efficiency of making either NHEJ-mediated indels or NHEJ-mediated deletions of small segments between two cuts. Over time, we expect to expand the repertoire of clinically feasible edits, including increasing larger NHEJ-mediated deletions and more complex, HDR-mediated edits. We also intend to develop the ability to achieve HDR-mediated replacement of entire DNA segments, which we believe will enable substantial expansion of the number of patients we can treat.



In this chart, each figure is intended to represent approximately 5,000 potential patients.

**Our Genomic Medicine Programs**

We have initiated a diversified range of research programs across multiple therapeutic areas. Since our scientific strategy is to optimize our genome editing platform in the context of specific product development efforts, we selected early programs requiring several different types of genome editing and DNA repair—both NHEJ and HDR. Furthermore, our initial programs use, and will allow us to further optimize, a range of delivery modalities such as local

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injection, including using an AAV vector, or *ex vivo* genome modification, where cells are removed from the body, edited, and given back to the patient.

We believe the therapeutic programs and delivery technologies we have chosen to date will demonstrate the depth and breadth of our ability to deploy our genome editing platform to treat patients in need. The current status of our programs is summarized in the table below:

Our Programs	Editing Mechanism	Delivery Mode	Commercial Rights	Discovery	IND
<b>Eye Diseases</b>					
Leber Congenital Amaurosis 10	NHEJ	AAV local injection	editas		Year-End 2017 Target
Genetic and Infectious Disease(s) of Eye <i>Usher Syndrome 2A, HSV-1</i>	NHEJ	AAV local injection	editas		
<b>Engineered T Cells</b>					
Gene Editing in T Cells to Treat Cancer	NHEJ	RNP <i>ex vivo</i>	Juno		
<b>Additional Research Programs</b>					
Non-Malignant Hematologic Diseases <i>Beta Thalassemia, Sickle Cell</i>	NHEJ, HDR	RNP <i>ex vivo</i>	editas		
Genetic Disease(s) of Muscle <i>Duchenne Muscular Dystrophy</i>	NHEJ	AAV, LNP	editas		
Genetic Disease(s) of Lung <i>Cystic Fibrosis</i>	NHEJ, HDR	AAV, LNP	editas		
Genetic and Infectious Disease(s) of Liver <i>Alpha-1 Antitrypsin Deficiency</i>	NHEJ, HDR	AAV, LNP	editas		

**Eye Diseases**

*Leber Congenital Amaurosis 10*

Leber Congenital Amaurosis, or LCA, is a heterogeneous group of inherited retinal dystrophies caused by mutations in at least 18 different genes and is the most common cause of inherited childhood blindness, with an incidence of two to three per 100,000 live births worldwide. Symptoms of LCA appear within the first year of life with significant vision loss, rapid involuntary movements of the eyes, painful eye response to bright light, and absence of measurable electroretinogram recordings due a lack of functional photoreceptor cells. Imaging studies of LCA patients have shown that the photoreceptor layer remains intact in the region of the fovea, a specialized region of the retina responsible for visual acuity, and that the intracranial visual pathways remain intact into early adulthood even though photoreceptor cells have already experienced damage. As a result, we believe that therapeutic approaches aimed at restoring function to the remaining photoreceptor cells could improve vision or arrest the further loss of vision in LCA patients, provided that treatment can be initiated prior to complete loss of photoreceptor cells.

The most common form of the disease, referred to as LCA10, is a monogenic disorder and represents approximately 20-30% of all LCA subtypes. LCA10 is caused by autosomal recessive mutations in the CEP290 gene, which encodes a protein required for the survival and proper function of photoreceptor cells. The most frequently found mutation within the CEP290 gene, occurring in approximately 85% of north and west European patients with LCA10, is an A to G nucleotide change that disrupts normal splicing, or processing, of the gene message, ultimately resulting in the generation of a smaller and nonfunctional protein. Decreased CEP290 protein leads to loss of photoreceptor function and cells over time, which leads to blindness.

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We assessed LCA10 comprehensively and found that it fits well with our genome editing approach and criteria for product development. These criteria include:

- *Medical need:* Currently, we are not aware of any approved treatment or potential therapy in clinical trials in either the United States or the European Union for LCA10, and severe to complete vision loss is the inevitable outcome for nearly all patients;
- *Opportunity for genome editing:* Gene therapy is not currently a viable approach to treating LCA10 because it requires delivery of the entire DNA coding sequence for CEP290, which is too large to fit into the best-characterized ocular gene therapy vector, AAV. In contrast, genome editing only requires delivery of the DNA coding sequence for the relevant Cas9-guide RNA complex, which can fit into AAV;
- *Nature of genetic mutation:* The A to G nucleotide change in the CEP290 gene is located in an intron, which is a portion of DNA that does not code for a protein. This allows genome editing via NHEJ with reduced risk of altering a protein coding sequence;
- *Delivery modality:* Sub-retinal AAV injection is the delivery mode for current gene augmentation therapy trials for related ophthalmic diseases and can be used for this program;
- *Pathophysiology of the disease and treatment window:* The photoreceptor cells that are responsible for daytime vision in LCA10 patients are largely non-functional and degenerate over time. By treating patients who retain some photoreceptor cells in the fovea, there is a window to repair the CEP290 gene and possibly improve vision or arrest further vision loss;
- *Safety and therapeutic index:* Because the eye is an immune-privileged location, injection directly beneath the retina of the eye minimizes the risk of a systemic toxic response by the immune system. In addition, because the product candidate will be delivered directly to the eye, there is likely to be minimal overall systemic exposure;
- *Clinical development path:* There are readily measurable endpoints such as visual acuity, retinal response to light, and optical coherence tomography that allow minimally invasive assessment of disease status;
- *Regulatory path:* There are no approved therapies for LCA10. We believe that the combination of clinically meaningful and readily measurable endpoints for diseases of vision, coupled with the unmet need in this orphan patient population, has the potential to enable an expedited regulatory process; and
- *Commercial opportunity:* LCA10 represents a focused market with a defined number of specialized centers treating the affected patients. We believe we can develop an effective small, targeted commercial infrastructure without the need for a commercial partner.

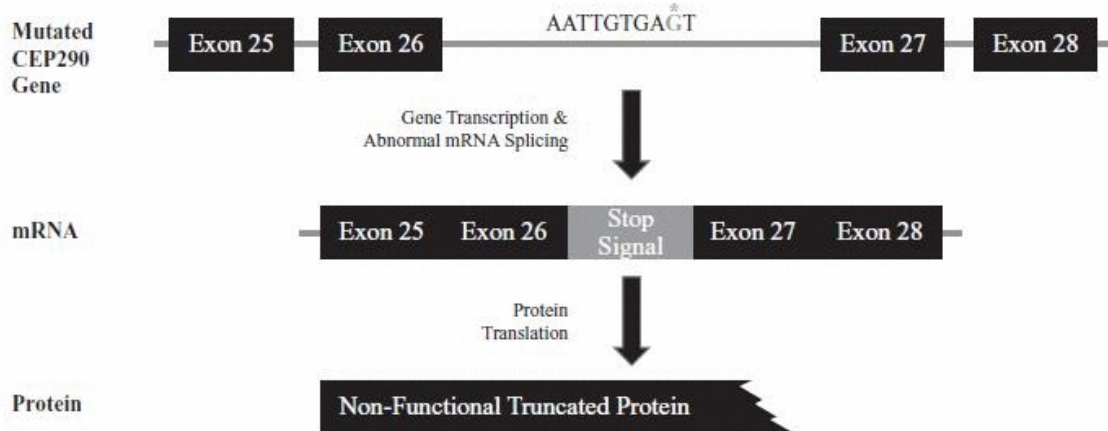
We are developing a genome editing therapeutic for LCA10 that uses an AAV vector to deliver the DNA encoding Cas9 and two guide RNAs to photoreceptor cells in the eye. In order to deliver this therapy directly and specifically to the site of disease, we are assessing the most well-established and relevant variants of AAV for retinal delivery. These variants have been shown by others to be effective delivery modalities in clinical trials for various other diseases, including retinal diseases.

Our approach is designed to eliminate the A to G nucleotide change in the CEP290 gene described above by cutting out that nucleotide and surrounding DNA, thus restoring normal protein expression and function of the remaining photoreceptor cells, which could improve or arrest the further loss of vision in LCA patients. The diagrams below illustrate the impaired protein expression that results from the LCA10 mutation and how we believe our approach can restore normal protein expression. As shown below, the LCA10 mutation consists of an A to G nucleotide change in the CEP290 gene that occurs in an intron located between exons 26 and 27 of the gene. Exons are regions of DNA that encode for segments of proteins. This mutation results in incorrect processing signals in the messenger RNA, or mRNA,

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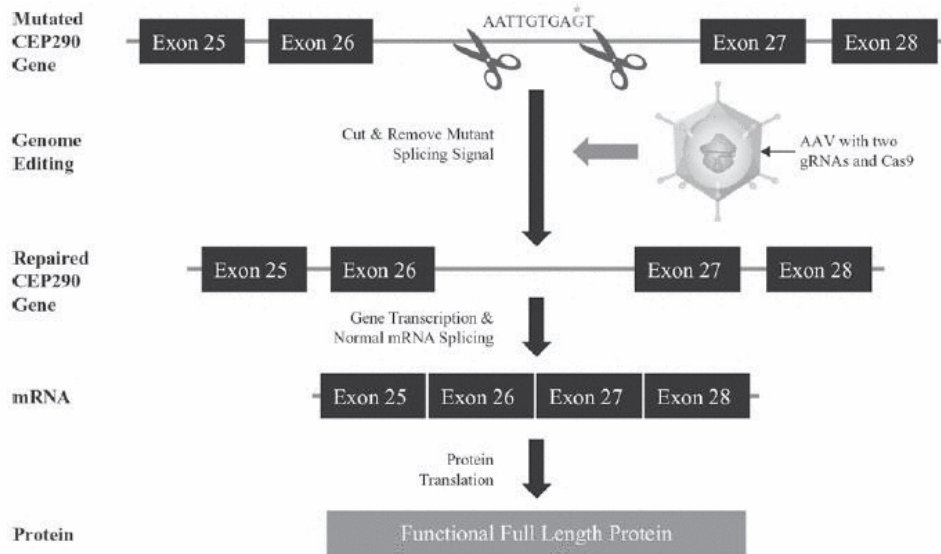
that is transcribed from the gene's DNA. This mRNA is then spliced, or processed, incorrectly, and this in turn leads to the inclusion of a premature stop signal, or codon, and the creation of a truncated and nonfunctional protein.

**Segment of CEP290 Gene with Mutation that Causes LCA10**



As shown below, our approach uses an AAV delivery vehicle containing a Cas9 nuclease and two guide RNA molecules designed to eliminate the mutation by cutting and removing it from the patient's genome. As a result, transcription of the edited DNA produces mRNA that no longer contains the premature stop codon, allowing for the production of functional protein.

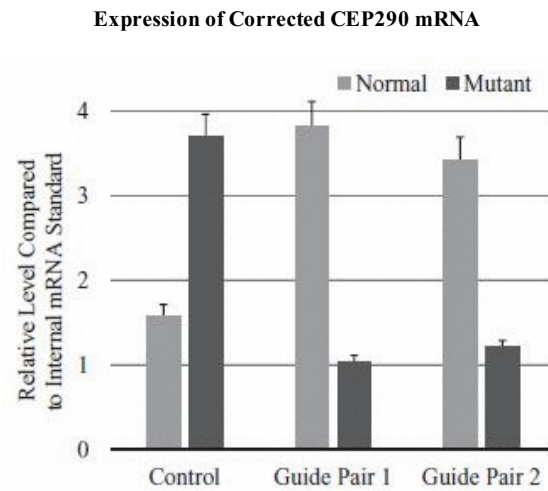
**Approach to Correcting the CEP290 Gene**





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We have tested combinations of Cas9 and guide RNA pairs in cells that were taken from patients with the CEP290 mutation to determine whether they could successfully edit the mutation and lead to correctly spliced mRNA and correctly produced CEP290 protein. We isolated and analyzed DNA from these edited cells and observed removal of the mutation-containing region in the DNA. Furthermore, as shown in the figure below, these studies also demonstrated that the edit restored significant levels of normal mRNA and lowered the levels of mutant mRNA, as compared to control. This restoration of normal, or wild type, mRNA expression suggests that we successfully corrected the LCA10 gene defect in these cells.



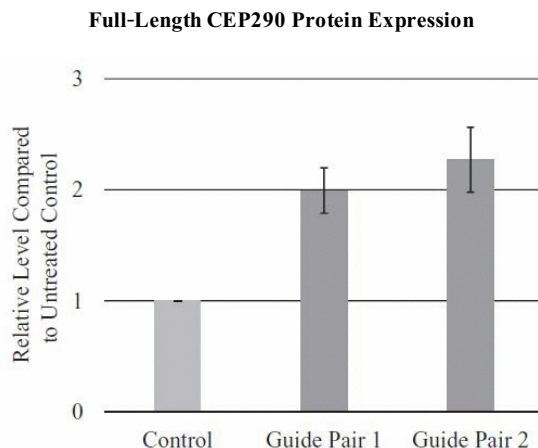
These results for guide pair 1 and guide pair 2 were statistically significant, with a p-value of less than 0.0001. P-value is a conventional statistical method for measuring the statistical significance of study results. A p-value of 0.05 or less represents statistical significance, meaning that there is a 1-in-20 or less statistical probability that the observed results occurred by chance.

In these studies we also observed two-fold and greater increases in full-length CEP290 protein expression compared to a control. We believe this demonstrates that successful editing of the genetic defect that causes LCA10 also



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leads to increased expression of the normal CEP290 protein. It is our view that increased expression of normal CEP290 protein could improve or arrest the further loss of vision in LCA10 patients.



To characterize editing specificity, we are applying a combination of methods to treated patient cells to quantify the frequency of modification at the targeted DNA location and to assess the potential for edits at off-target locations. We believe our detailed characterization of editing specificity *in vitro* will allow us to select guide RNA and endonuclease combinations with the highest likelihood of providing clinical benefit in patients.

In addition, in a non-human primate preclinical study, we demonstrated *in vivo* proof-of-editing in the retina following subretinal injection of a preclinical version of our product candidate. We believe this study is an initial indication of the therapeutic potential of our product candidate. We aim to initiate a clinical natural history study in mid-2017 to evaluate the clinical course and characteristics of LCA10 more extensively, and we aim to file an IND application by the end of 2017 for our LCA10 program.

*Other Eye Diseases*

We also intend to pursue the development of therapies for eye diseases other than LCA10, including Usher Syndrome 2A, or USH2A, and Herpes Simplex Virus 1, or HSV-1, infections. We believe that our experience with the LCA10 program will support the development of therapies for these other eye diseases. For example, the successful construction, packaging, and testing of the components of the AAV vector we are pursuing for LCA10 will continue to inform our approach to treating USH2A.

*Usher Syndrome 2A*

USH2A gene mutations are the most common cause of Usher syndrome, a form of retinitis pigmentosa. The U.S. population prevalence of Usher syndrome is estimated to be one in 6,000 individuals, and USH2A gene mutations account for an estimated 25-30% of all cases of Usher syndrome. Loss of the usherin protein encoded by the USH2A gene leads to a degeneration of the retina and progressive vision loss. More than 200 mutations have been identified for this gene. Our initial goal in this research program is to address mutations within exon 13, which is the location of the highest percentage of USH2A gene mutations.

*Herpes Simplex Virus 1*

Herpes Simplex Virus 1, or HSV-1, causes lifelong infections mainly leading to ocular and oral disease. Infected individuals develop persistent latent infections, mainly in the nerves in the affected part of the body. During

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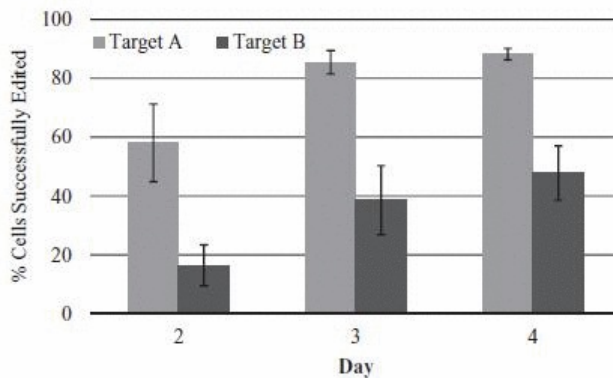
latency, the HSV-1 DNA does not integrate into the infected individual’s genome but it remains within the individual’s cells as independent viral genomic material. The latent HSV-1 virus can then be reactivated by illness, emotional or physical stress, and other conditions. Ocular infection with HSV-1 is a major health problem, especially in developed countries. It is the most common infectious cause of blindness in the United States with over 35,000 new cases each year. Existing therapies have not been shown to be beneficial in preventing initial HSV-1 infection or recurrences. As a result, there is a need for an effective therapy that prevents or reduces reactivation of latent HSV-1. We plan to deliver the CRISPR molecular machinery to the eye and specifically cleave and inactivate latent HSV-1 DNA with the goal of eliminating or reducing reactivation.

**Engineered T Cell Therapies for Immuno-Oncology**

Engineered T cells have shown encouraging early clinical activity against multiple cancers, and there is significant interest in the medical community in expanding the application of this technology across a broader range of cancers and patients. Recent data suggest that improving T cell persistence, or the duration these cells are active in the body, positively correlates with anti-tumor activity. We believe that our genome editing technology has the potential to improve T cell persistence and confer other advantageous properties on engineered T cells, such as overcoming signals in the tumor microenvironment that reduce T cell activity. If we are successful, genome-edited engineered T cells have the potential to significantly expand the types of cancers treatable by chimeric antigen receptor/T cell receptor, or CAR/TCR, engineered T cells and to improve the outcomes of these therapies.

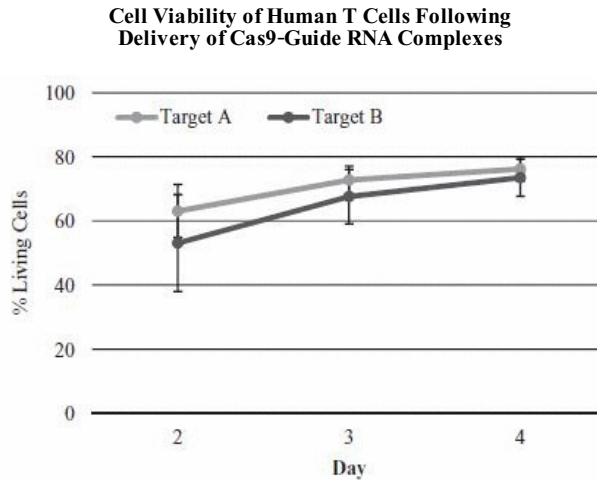
Through our collaboration with Juno Therapeutics, a leader in the emerging field of immuno-oncology, we plan to direct our genome editing technology towards multiple targets in order to improve the efficacy and safety of CAR/TCR engineered T cells against a range of tumor types. We are currently optimizing genome editing components and delivery methods compatible with engineered T cell manufacturing methods developed by Juno Therapeutics. In an *in vitro* study under this collaboration, Cas9-guide RNA complexes directed against two different T cell target genes were delivered into human T cells obtained from three separate donors. At different time points, the extent of genome editing and the percentage of viable cells were measured. We assessed editing by measuring protein expression on the cells’ surfaces following treatment with our Cas9-guide RNA complexes. We observed high levels of editing, achieving approximately 90% for target A and 50% for target B, across samples from the three donors on day four, as shown in the figure below.

**Editing of T Cell Target Genes in Human T Cells**



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In addition, we observed on average approximately 75% cell viability four days following delivery, as shown in the figure below. We believe this is a sufficiently favorable result to support further advancement of this program.



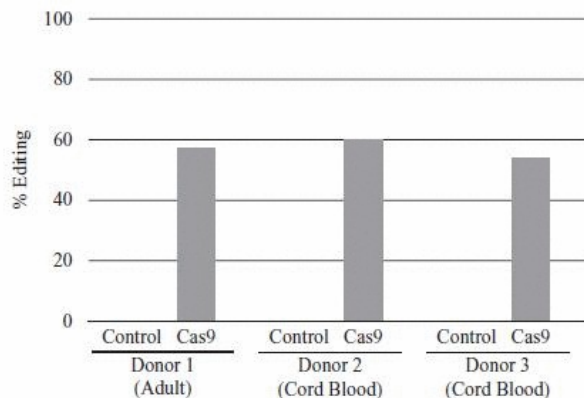
We and Juno Therapeutics have selected a number of targets for editing using both NHEJ- and HDR-based approaches to evaluate the effects on safety and efficacy of CAR/TCR engineered T cells, both *ex vivo* and *in vivo*. These studies are designed to facilitate the selection of therapeutic programs to be pursued under our collaboration with Juno Therapeutics.

**Additional Research Programs**

*Non-malignant Hematologic Diseases*

We intend to develop approaches for genome editing in hematopoietic stem cells to support the advancement of other programs to treat non-malignant hematological diseases. We are investigating the correction of the human beta globin, or HBB, gene in order to treat genetic disorders such as beta thalassemia and sickle cell disease. In an *ex vivo* study, Cas9-guide RNA complexes directed against the HBB gene were delivered into hematopoietic stem cells obtained from three separate healthy donors and evaluated against untreated control cells to assess editing activity as well as effects on the cells' viability, proliferation, and ability to differentiate into different types of blood cells. As shown in the figure below, we observed approximately 55-60% editing of the HBB gene in cells treated with Cas9-guide RNA complexes as compared to no editing observed in the control cells. We observed no substantial differences between the treated cells and the untreated control cells in their viability, proliferation, or ability to differentiate into different types of blood cells.

***ex vivo* Editing of Hemoglobin Beta Gene  
in Human Stem Cells**



In addition to our work on the HBB gene, we are also pursuing additional gene editing approaches to treating sickle cell disease and beta thalassemia. Furthermore, we are actively assessing other opportunities to develop medicines for diseases where we believe gene editing of hematopoietic stem cells is likely to produce a therapeutic effect.

We believe advances developed through our collaboration with Juno Therapeutics, including our efforts to optimize genome editing components and delivery methods compatible with engineered T cells, may support our current and future non-malignant hematologic disease programs.

*Duchenne Muscular Dystrophy*

Duchenne muscular dystrophy, or DMD, is a genetic disorder primarily affecting boys and is characterized by progressive muscle weakness and atrophy that presents in early childhood and rapidly results in loss of ambulation and respiratory muscle function. Additionally, DMD often causes cardiomyopathy in adolescence. Death occurs typically in early adulthood. The incidence of DMD is approximately one in every 3,500 male births with a prevalence of approximately 15,000 cases in the United States. The FDA has approved only one therapy for the treatment of DMD, which may treat approximately 13% of patients. The current standard of care consists of palliative measures such as glucocorticoids and physical therapy as well as braces, wheelchairs, spinal surgeries for scoliosis, and mechanical ventilation. The disease is caused by mutations in the gene that encodes dystrophin, a structural protein that is important for normal muscle health. Loss of dystrophin function leads to muscle degeneration. We believe that restoring dystrophin activity before the onset of severe loss of muscle function could significantly and favorably alter disease progression.

The dystrophin gene is one of the largest in the human genome spanning 2.2 million base pairs. Pathogenic mutations can occur throughout the gene. Many disease-causing mutations in the dystrophin gene consist of deletions that lead to non-functional protein. Interestingly, large deletions in the middle of the dystrophin protein have been identified that cause only mild to moderate disease. For example, deletions of selected exons have been shown to cause the much less severe Becker muscular dystrophy. Our genome editing approach is to introduce targeted deletions of mutation-containing segments of the gene in order to create smaller, yet functional versions of the dystrophin gene. Based on the known spectrum of DMD-causing mutations, an NHEJ-mediated small deletion of exon 51 would be expected to address approximately 13% of patients whereas an NHEJ-mediated large deletion encompassing exons 45 through 55 would expand coverage to up to 60% of patients.

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### *Cystic Fibrosis*

Cystic fibrosis, or CF, is the most common lethal autosomal recessive disease in the Caucasian population. The overall birth prevalence of CF in the United States is approximately one in 3,700. While several organs are affected, the morbidity and mortality is primarily caused by the severity of lung disease. The gene that causes CF encodes the cystic fibrosis transmembrane conductance regulator, or CFTR, which helps maintain the water balance within the lung. Mutations in the CFTR gene lead to an imbalance of ion and water movement, leading to accumulation of mucus, chronic bacterial infection and inflammation of the airway epithelium. Our genome editing approach is premised on deleting, through NHEJ, a very rare mutation within the CFTR gene. We then intend to leverage that learning to embark on a more technologically challenging approach of correcting, through HDR, the rF508 mutation, which is present in approximately 70% of all CF patients. Correcting the CF mutations in lung epithelial cells will require efficient editing of these cells and development of advanced pulmonary delivery modalities. We plan to establish multiple collaborations with academics, foundations, and other companies developing novel lung delivery approaches to achieve these goals. To that end, in May 2016 we entered into an award agreement with Cystic Fibrosis Foundation Therapeutics, Inc., or CFFT, pursuant to which CFFT has agreed to pay us up to \$5.0 million over the agreement's three year term to support our CF development program and related technology research and development. Under the terms of the agreement, we are required to contribute additional funds to the program in an amount equal to the funds contributed by CFFT and to pay certain amounts to CFFT upon the achievement of specified events.

### *Alpha-1 Antitrypsin Deficiency*

Alpha-1 antitrypsin deficiency is a genetic disease that causes defective production of the Alpha-1 Antitrypsin, or A1AT protein, leading to lung and liver disease. A1AT is one of the primary proteins made in the liver and protects the lungs from pro-inflammatory enzymes. This disease affects about one in 1,500 to 3,500 individuals of European ancestry. Mutations in A1AT lead to accumulation of A1AT aggregates and result in liver and lung disease. The current standards of care are weekly intravenous infusions of functional A1AT protein obtained from human donor plasma, and lung or liver transplant for severe cases. Our genome editing approach starts with deleting, through NHEJ, the gene in the liver to prevent liver disease, followed by gene correction in the liver to address both liver and lung disease.

### **Our Genome Editing Platform in Detail**

We are developing a proprietary genome editing platform consisting of four interrelated components that are designed to address four key goals of genome editing:

- create a comprehensive toolbox for robust and selective genome engineering;
- provide efficient and targeted delivery to any tissue or cell;
- effect spatial and temporal control of gene editing and specificity; and
- orchestrate the cellular response to ensure accurate and precise genome editing.

We believe that the developments we have made in our genome editing platform position us to be able to identify and develop innovative genome editing therapies targeting a wide variety of genetically defined diseases. All of our programs to develop medicines leverage aspects of this platform while also providing insights that help improve our ongoing and future drug development capabilities. We believe our genome editing platform forms the basis for our ongoing leadership in the field and differentiates us from other companies working in genome editing.

### *Nuclease Engineering*

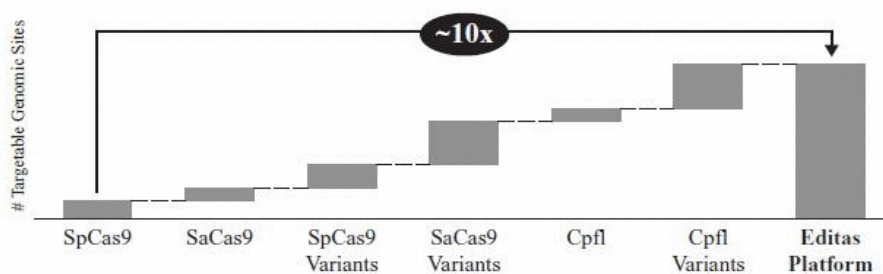
We use our genome editing platform to identify and optimize both the enzyme, including Cas9 and Cpf1, as well as advanced forms of each, and the guide RNA molecule, to create what we believe will be the optimal endonuclease-guide RNA complex for a given disease target. We have made substantial advances in the characterization

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and modification of different natural and engineered variants of Cas9 and Cpf1 enzymes and in the design, synthesis, modification, analysis, and characterization of guide RNAs. We believe the diversity of the Cas9 and Cpf1 enzymes that we are currently employing and those that we are continuing to further develop have the potential to provide us with a competitive advantage as we develop a range of products with different technical needs. We believe our systematic approach to measurement of both the efficiency and specificity of multiple possible enzyme and guide RNA combinations enables us to optimize the identification of lead molecules to progress into more advanced testing. Our aim is to continue to develop new engineered Cas9 and Cpf1 enzymes with altered PAM specificities, different DNA cutting capabilities, and additional advanced properties. For example, we are using directed evolution, a form of guided protein engineering, to develop Cas9 enzymes that recognize different PAMs in order to target additional locations in the genome. We are also developing Cas9 enzymes that can cut DNA in an allele-specific manner. We believe that further developing our nuclease engineering capabilities will allow us to further broaden the range of diseases we can treat while at the same time ensuring that our products have the best possible safety profiles.

We have characterized different Cas9 and Cpf1 enzymes for several reasons. Firstly, a smaller enzyme will have advantages for delivering the endonuclease using a viral vector due to the inherent size limitations of most such delivery systems. For example, the Cas9 enzyme from *Staphylococcus aureus* is significantly smaller than that from *Streptococcus pyogenes* (3,159 vs. 4,104 base pairs), and this is important when working with AAV as a delivery vector, which has an effective packaging limit of approximately 4,700 base pairs. Secondly, identifying Cas9 and Cpf1 enzymes with different editing properties will expand the number of potential editing sites in the human genome. As shown below, the range of natural and engineered variants of Cas9 and Cpf1 have significantly expanded the number of sites in the human genome that we can potentially target. As compared to the most commonly used, naturally occurring version of Cas9, from the bacterial species *S. pyogenes*, the range of endonucleases in our platform can target approximately ten times as many genomic sites.

### Comparison of Number of Genomic Sites Targetable by Various Enzymes and Variants



In order to accelerate and standardize the selection of guide RNAs, we have created proprietary analytical software that supports guide RNA design through single nucleotide polymorphism analysis, specificity prediction, and assessment of relative importance of potential off target sites. We have also advanced the engineering of guide RNAs such that we are able to produce molecules with suitable properties for use in human cells which have the potential to reduce the innate immune response associated with foreign RNA. This, coupled with active, purified protein enables efficient genome editing for *ex vivo* applications in human cells and has the potential to improve the safety and efficacy of the medicines we develop.

### Delivery

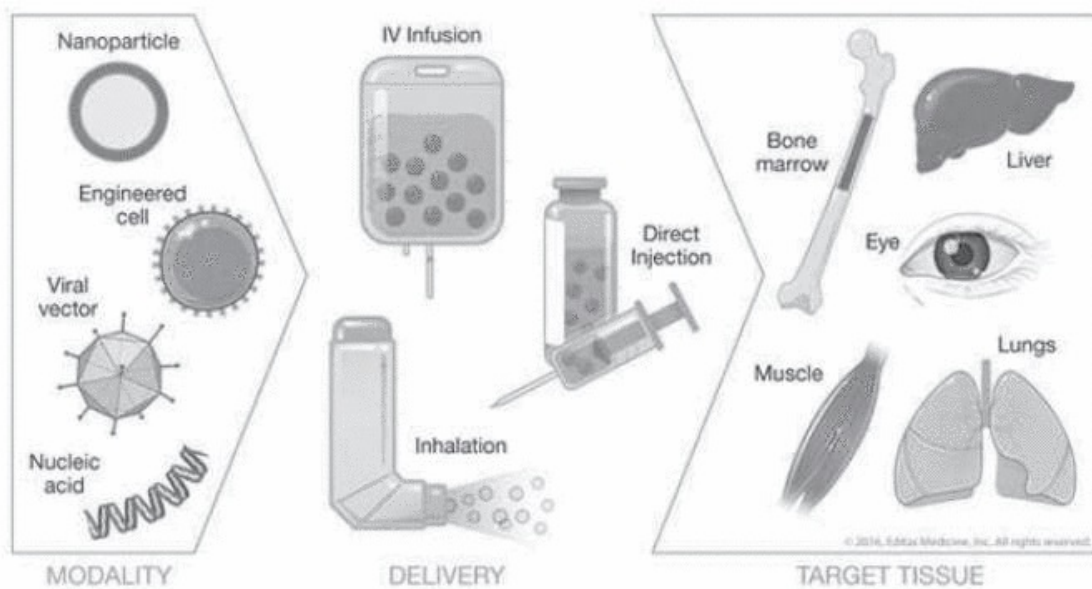
An appropriate product configuration must be designed and optimized to provide efficient and tightly controlled delivery to the desired tissue or cell type. Two important elements of delivery are the mode of delivery to the cell and the type of molecule delivered.

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There are three types of molecules that we can deliver to a cell to effect genome editing:

- **DNA.** If DNA is delivered, both the DNA that codes for Cas9 or for Cpf1 along with DNA that codes for the guide RNA(s) must be introduced into the cell. The cell can then use these DNA molecules to make the Cas9 or Cpf1 enzyme and the guide RNA(s) and assemble them into the desired endonuclease-guide RNA complex so this complex can then locate its target(s) in the cell's genome and make the relevant edit(s).
- **RNA.** If RNA is delivered, both the mRNA that codes for Cas9 or for Cpf1 along with the guide RNA(s) must be introduced into the cell. The cell can then use the mRNA to make the Cas9 or Cpf1 enzyme and assemble it with the guide RNA(s) to produce the desired endonuclease-guide RNA complex so this complex can then locate its target(s) in the cell's genome and make the relevant edit(s).
- **RNP.** Finally, if a pre-formed RNP complex is delivered, the cell is provided with an already-functional endonuclease-guide RNA complex that is ready to act on target sites in the genome.

The mode of delivery for the different endonuclease-guide RNA complexes depends on the type of molecule (DNA, RNA, or RNP) that is delivered. Delivery can be performed through a range of approaches such as local or systemic injection *in vivo* or through *ex vivo* genome modification where cells are removed from the body, edited, and the engineered cells are given back to the patient. Delivery mode options depend on whether a therapy is being delivered *in vivo* or *ex vivo* and can include viral vectors, such as AAV, lipid nanoparticles, engineered cells, and nucleic acids. As shown below, these potential product configurations can be administered through intravenous infusion, a direct injection into a target tissue or organ, or by inhalation.

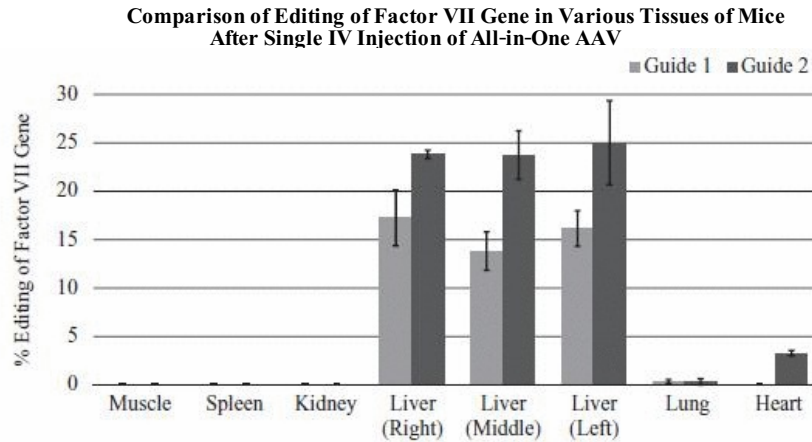


The delivery component of our genome editing platform aims to identify and develop delivery vehicles both by leveraging existing technologies, such as the electroporation system commercialized by MaxCyte, Inc., and also investing in new approaches that have the potential to be used to treat many diseases over the longer term. To this end, we have taken advantage of the smaller *S. aureus* Cas9 and existing AAV technology to construct an “all-in-one” viral vector that is able to deliver the DNA coding for the nuclease protein and one or two guide RNAs directly to cells. We

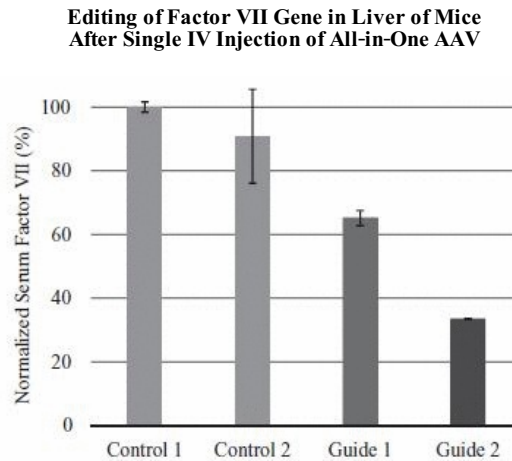
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believe our ability to configure all the components for genome editing in an “all-in-one” AAV vector has substantial advantages for manufacturing and delivery compared to approaches that rely on multiple vectors.

As part of our work to establish our ability to modify genes in the liver *in vivo*, we have successfully delivered an all-in-one AAV vector encoding *S. aureus* Cas9 and a guide RNA and demonstrated efficient editing of the Factor VII gene, a target in the liver, in mice. In these experiments we evaluated three different AAV vector constructs against a control solution, which we refer to as Control 1, in each case administered by injection into the blood stream. The AAV vectors evaluated in the experiments delivered either an inactive control protein, which we refer to as Control 2, *S. aureus* Cas9 and a selected Factor VII guide RNA, which we refer to as Guide 1, or *S. aureus* Cas9 and a second selected Factor VII guide RNA, which we refer to as Guide 2. In these experiments, we observed editing of the DNA for the Factor VII gene in liver tissue with low levels of editing in tissues other than the liver, as shown in the figure below.



In addition, we observed a significant reduction in serum levels of Factor VII by each of the two different guide RNAs targeting this gene, as shown in the figure below.





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We believe these data represent an important proof of concept for our ability to develop genome editing medicines that can be delivered to the liver by systemic administration. In addition, the results of this study also provide a framework by which to benchmark different systemic delivery modalities designed to target a range of genes expressed in the liver.

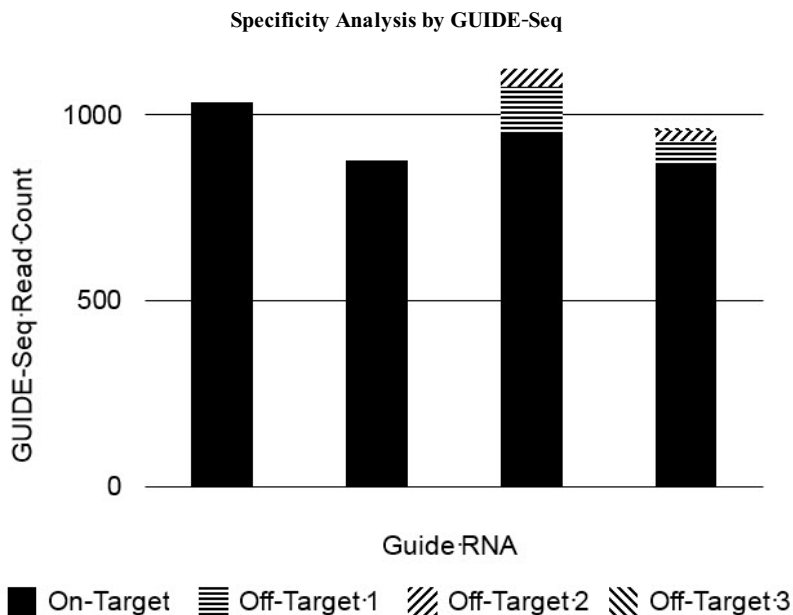
We have also made substantial advances in the *ex vivo* delivery of CRISPR systems to mature human T cells and hematopoietic stem cells derived from the bone marrow. We have been able to demonstrate approximately 90% *ex vivo* editing in human T cells and greater than 45% *ex vivo* editing in hematopoietic stem cells using either mRNA or RNP complexes. These results are consistent across multiple cell donors and multiple target genes. We believe this supports the view that there are multiple delivery approaches that can be used to develop medicines for diseases of the blood and bone marrow.

### *Control and Specificity*

Control of cellular exposure to the endonuclease-guide RNA complex and specificity of the DNA cut are important to optimizing the location and duration of editing activity. We believe these features are critical to designing medicines that are both safe and effective, and we are developing and applying technologies in these areas. We strive to identify, measure, and eliminate off-target activity in a systematic and scalable manner as we optimize our molecules. To accomplish this, we have combined multiple orthogonal methods in the design, testing, and optimization process. Our strategy to assess specificity during the research stage includes:

- *Establish industry-leading computational tools to design guide RNAs.* The guide RNA activates and directs the Cas9 or Cpf1 enzyme to the right cutting position in the genome. It is important for the guide RNA to be highly selective to ensure that the right site is cut. For every guide RNA we test, we compare the targeted DNA sequence to the sequence of the entire human genome to identify all sequences that have significant similarity to the targeted DNA sequence. Based on our internal algorithms, we eliminate any guide RNAs that have certain defined degrees of similarity to other sites across the genome. We continually refine our guide RNA design algorithms based on results from large-scale guide RNA screens and further confirmation and refinement experiments. We expect that this will enhance our ability to design efficient and specific guide RNAs as our database expands over time.
- *Use multiple unbiased, comprehensive methods to empirically assess specificity in vitro.* While computational tools are helpful, they are only a starting point and are insufficient to understand specificity completely. It is critical to make and test molecules in unbiased assays to assess the specificity of their activity. We intend to use multiple methods to empirically assess specificity in order to test for a variety of potential off-target cuts, at sites both similar and dissimilar to the targeted DNA site. For example, we have implemented in our laboratories a method called GUIDE-Seq, which was developed by one of our founders and works in cells *in vitro*. The GUIDE-Seq method identifies potential off-target cuts in DNA by inserting a small, unique piece of synthetic DNA at breaks in the cell's genome and then sequencing the cell's DNA near the site of insertion. A "read" is generated each time the unique piece of inserted DNA is mapped to the cell's genome. The genomic location of the "read" indicates whether a cut was made at the intended site or at an off-target site. We have used the GUIDE-Seq method to assess the specificity of different guide RNAs targeted to the same gene. In one experiment, we evaluated four different Cas9-guide RNA complexes targeted at a single gene and observed that two of the Cas9-guide RNA complexes were able to produce targeted cuts in the DNA with no apparent off-target cut sites while the third produced two

different types of off-target cuts and the fourth produced three different types of off-target cuts, as shown in the figure below.



We are applying this method to our early programs, including our LCA10 and engineered T cell programs. In addition, we are expanding our capabilities to include techniques other than GUIDE-Seq to assess specificity empirically.

- *Create validated assay panels composed of potential off-target sites identified by both computational approaches and the use of other unbiased methods.* These targeted resequencing assay panels will then be applied to *in vitro* and *in vivo* experimental systems to confirm specificity as we advance to the clinic.

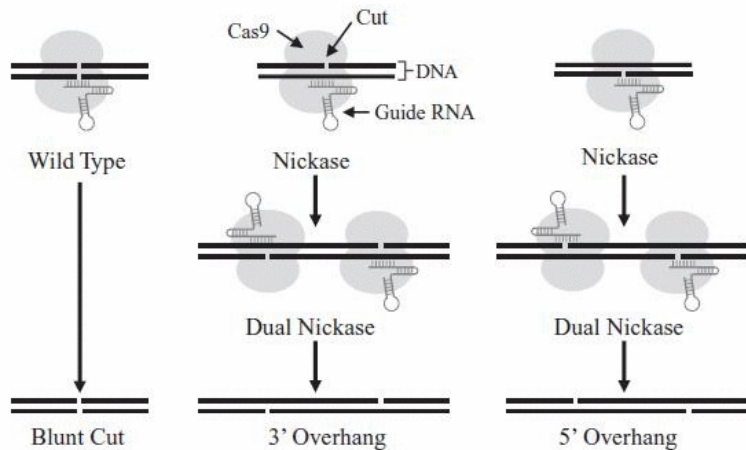
To optimize the specificity of any product candidate we may develop, there are a number of different aspects of the product configuration that we will refine in addition to the sequence of the guide RNA. The length of the guide RNA, the type of Cas9 or Cpf1 enzyme, the delivery vector, the use of tissue-selective promoters, and the duration of exposure all contribute to overall specificity, and we optimize each of these elements for every program. We have evaluated various forms of Cas9 enzymes and different promoters for selective expression in different cell types and plan to do the same for the Cpf1 enzyme, which we believe have the potential to increase the tissue specificity of our medicines. We have also identified and characterized an alternate promoter system for the expression of guide RNAs to selectively enhance editing activity in targeted tissues and implemented and produced a detailed characterization of multiple distinct approaches to specificity evaluation in order to best characterize the specificity of our genome editing approaches. To reduce the persistence of genome editing activity, we are developing self-regulating genome editing systems designed to deliver not only the endonuclease-guide RNA complex, but also an “off switch” that reduces the presence of the endonuclease-guide RNA complex over time. We have completed studies of these systems that demonstrate the ability to both maintain on-target editing and also reduce levels of editing components once the on-target edit is likely to have been completed.

There are different mechanisms that a cell can use to repair cuts in DNA. Each mechanism results in different kinds of genetic changes. The two major DNA repair mechanisms are NHEJ and HDR. We are developing approaches to selectively harness these DNA repair mechanisms to be able to drive the appropriate type of repair for a given disease. In particular, a significant part of our effort to expand our platform is to develop methods to better direct the HDR mechanism. We are taking several approaches to improve our understanding of HDR-based DNA repair and to develop tools to influence it. The ability to direct the DNA repair mechanism is critical to achieving the broadest potential for our platform.

Our initial work in directed editing has focused on the gene for HBB, which is mutated in beta thalassemia and sickle cell disease. We have investigated how different kinds of DNA cuts by a CRISPR molecule drive the choice of DNA repair mechanism used by the cell to repair these cuts. These experiments took advantage of the flexibility of CRISPR targeting as well as a series of engineered variants of the Cas9 enzyme that either cut one or both strands of the DNA double helix. The wild type Cas9 enzyme cuts both strands of DNA. Engineered variants of the Cas9 enzyme that only cut one of the two strands are called nickases. In experiments in cells, we used three different versions of the Cas9 enzyme and we designed guide RNAs to direct them to make three kinds of cuts in the HBB gene:

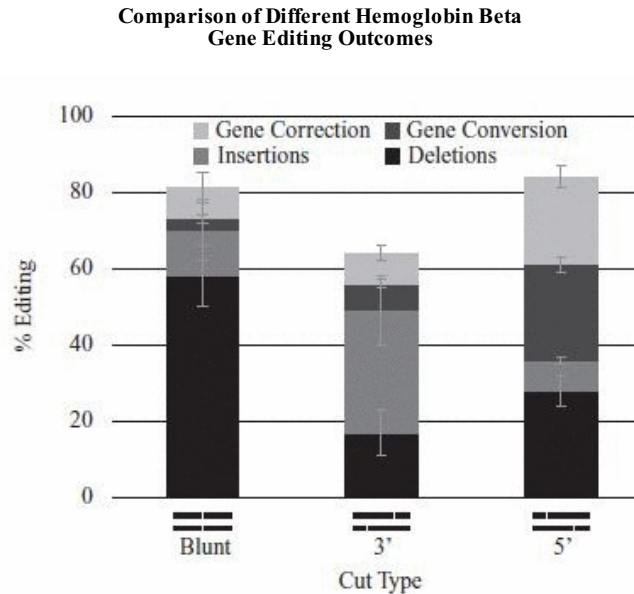
- *Blunt-Ended DNA Cut:* We used the wild type Cas9 enzyme with a single guide RNA to create a cut through both strands of the DNA double helix in the same place, leaving what is referred to as a blunt end (left figure below).
- *3' Overhang DNA Cut:* We designed two “bottom strand” Cas9 nickases so that each nickase cuts one strand of the DNA double helix and the respective guide RNAs directed them to opposite sides of the helix. These single-stranded cuts in the DNA were offset from one another by a short distance and resulted in what is termed a 3' overhang (middle figure below).
- *5' Overhang DNA Cut:* We designed two “top strand” Cas9 nickases so that each nickase cuts one strand of the DNA double helix and the respective guide RNAs directed them to opposite sides of the helix. Once again, these single-stranded cuts in the DNA were offset from one another by a short distance. In this case, the use of two offset, top strand nickases resulted in what is termed a 5' overhang (right figure below).

**Schematic of Experiment Testing Role of Cut Type in HDR**



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We applied these Cas9-guide RNA complexes to cells and assessed how the cells repaired their DNA as measured by editing of DNA for the HBB gene. In addition, we included in these studies an extra piece of DNA called a repair template. This DNA, or ssODN, contained a DNA sequence that we could detect so that we could determine if the cell used the ssODN piece of DNA in the repair process. The results of this experiment are shown in the figure below.



These studies demonstrated that the cells used different DNA repair mechanisms to edit the HBB gene depending on the type of DNA cut. Importantly, in response to a 5' overhang cut, the cells used the HDR process much more often than in response to the other types of cuts. The cells used the experimentally supplied ssODN piece of DNA as the template for HDR fairly frequently (23%). In addition, there was a relatively high frequency (25%) of a phenomenon known as gene conversion. In the case of gene conversion, the template for repair was the gene for hemoglobin delta, or HBD, a gene that is physically close to and highly similar to the HBB gene.

These results show the flexibility of CRISPR technology in creating multiple cut types and demonstrate that different cut types can result in profoundly different gene repair outcomes. In addition, the observed use of nearby very similar DNA from the HBD gene sequences suggests that a more generalizable approach to gene correction may be possible by designing cuts that drive cells to repair mutations from pre-existing DNA sequences that are appropriately co-located. Based in part on these observations, we are seeking to drive HDR-based repair by developing engineered DNA repair templates as well as tethering DNA repair templates to the endonuclease-guide RNA complex. We believe that our ability to understand and harness the editing mechanisms used by cells creates opportunities to improve our existing programs and opens up new opportunities to develop medicines.

**Juno Therapeutics Collaboration and License Agreement**

In May 2015, we entered into a collaboration and license agreement with Juno Therapeutics for the research and development of engineered T cells with chimeric antigen receptors, or CARs, and T cell receptors, or TCRs, that have been genetically modified to recognize and kill other cells. In particular, Juno Therapeutics and we will research and develop CAR and TCR engineered T cell products across three research programs over a five-year period, ending on May 26, 2020. Juno Therapeutics has the option to extend the research period through May 26, 2022, upon payment of one-year extension fees in the mid-single-digit millions of dollars per year. We refer to the five- to seven-year period as the research program term of the collaboration.

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During the research program term, we are responsible for generating genome editing reagents that modify gene targets selected by Juno Therapeutics. Juno Therapeutics is responsible for evaluating and selecting for further research and development CAR and TCR engineered T cell products modified with our genome editing reagents. Except for our obligations under the mutually agreed research plan, Juno Therapeutics has sole responsibility, at its own cost, for the worldwide development, manufacturing, and commercialization of the selected CAR and TCR engineered T cell products for the diagnosis, treatment, or prevention of any cancer in humans, excluding the diagnosis, treatment, or prevention of medullary cystic kidney disease 1, or the Exclusive Cas9-I Field.

Under the collaboration agreement, we granted to Juno Therapeutics an exclusive (even as to us), worldwide, milestone and royalty-bearing, sublicensable license to certain of our owned and in-licensed patent rights to research, develop, make, have made, use, offer for sale, sell and import selected CAR and TCR engineered T cell products in the Exclusive Cas9-I Field. In addition, we granted to Juno Therapeutics a non-exclusive, worldwide, milestone and royalty-bearing, sublicensable license to certain of our owned and in-licensed patent rights to use genome editing reagents that are used in the creation of a CAR or TCR engineered T cell product on which Juno Therapeutics has filed an IND for the treatment or prevention of a cancer in humans for researching, developing, making, having made, using, offering for sale, selling, and importing that CAR or TCR engineered T cell product in all fields outside of the Exclusive Cas9-I Field, excluding the diagnosis, treatment, or prevention of medullary cystic kidney disease 1. We further granted to Juno Therapeutics a non-exclusive, worldwide, non-sublicensable license to certain of our owned and in-licensed patent rights to, among other things, conduct the activities assigned to Juno Therapeutics under the mutually agreed research plan and to our genome editing reagents for further research and development of CAR and TCR engineered T cell products. Juno Therapeutics granted to us a non-exclusive, worldwide, royalty-free, and non-sublicensable license to certain Juno Therapeutics patents solely for the purpose of our conducting the research activities assigned to us under the mutually agreed research plan.

During the research program term and except pursuant to the collaboration agreement, we may not conduct or participate in, and may not license, fund or otherwise enable a third party to conduct or participate in, research, development, manufacture, or commercialization of CAR and TCR engineered T cells in the Exclusive Cas9-I Field. In addition, we may not enter into any collaboration, license, or other relationship with a third party to use our genome editing technology with respect to CAR and TCR engineered T cells in any other field, excluding the diagnosis, treatment, or prevention of medullary cystic kidney disease 1, unless we first provide written notice to Juno Therapeutics and provide Juno Therapeutics an opportunity to discuss a comparable collaboration, license, or other relationship. Juno Therapeutics has agreed to certain exclusivity obligations with us with respect to certain gene editing technologies.

During the term of the collaboration agreement and except pursuant to the collaboration agreement, we may not conduct or participate in, and may not license, fund, or otherwise enable a third party to conduct or participate in, research, development, manufacturing, or commercialization activities involving the use of our genome editing technology, or any genome editing technology similar to ours, with respect to the gene targets selected by Juno Therapeutics during the research program term for further research and development in the Exclusive Cas9-I Field. During the term of the collaboration agreement and except pursuant to the collaboration agreement, we may not conduct or participate in, and may not license, fund, or otherwise enable a third party to conduct or participate in, research, development, manufacturing, or commercialization activities with respect to a certain type of CAR or TCR engineered T cell product for use in the Exclusive Cas9-I Field, where such product targets a protein designated by Juno Therapeutics during the research program term as a target for Juno Therapeutics' further research and development of that certain type of CAR or TCR engineered T cell product.

Juno Therapeutics and we each must use diligent efforts to perform all activities for which Juno Therapeutics or we are responsible under the collaboration. Juno Therapeutics also is required to achieve certain regulatory objectives with respect to the engineered T cells in each of the three programs by specified dates. Under the agreement, if Juno Therapeutics does not meet its initial regulatory objective by the required date with respect to an engineered T cell in a specified program, then we can, as our exclusive remedy to Juno Therapeutics' failure, convert the exclusive license we granted to Juno Therapeutics to a non-exclusive license to Juno Therapeutics with respect to the particular program to which Juno Therapeutics' failure relates. If Juno Therapeutics does not meet a subsequent regulatory objective with respect to an engineered T cell within a program, then we can, as our exclusive remedy to Juno Therapeutics' failure,

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convert the exclusive license we granted to Juno Therapeutics to a non-exclusive license to Juno Therapeutics with respect to the particular engineered T cell to which Juno Therapeutics' failure relates.

The collaboration is supervised by a joint research committee, or JRC, comprising an equal number of representatives from each of Juno Therapeutics and us. The JRC oversees and coordinates research activities during the research program term. Moreover, each party will appoint a project leader and the project leaders will be responsible for, among other things, coordinating the day-to-day work and raising cross-party disputes in a timely manner. Decisions of the JRC are made by unanimous vote, with each of Juno Therapeutics and us having one vote. If the JRC is not able to reach a unanimous decision, Juno Therapeutics' and our respective chief executive officers will attempt to resolve the dispute in good faith. If the chief executive officers cannot resolve the dispute, subject to certain requirements, Juno Therapeutics has the final decision making authority with respect to disputes relating to the development of the licensed products within the research plan, and we have the final decision making authority with respect to disputes relating to our patents, know-how and technology.

Under the terms of the collaboration agreement, we received an upfront payment of \$25.0 million from Juno Therapeutics and in the second quarter of 2016 we received our first milestone payment of \$2.5 million under the collaboration for technical progress in a research program. In addition, we have the potential to receive up to \$22.0 million in research support over a five year term across the three programs under our collaboration, subject to adjustment in accordance with the terms of the agreement, of which we had recognized \$4.8 million as of December 31, 2016. We are eligible to receive future research and regulatory milestones of approximately \$160 million for each of the first products developed in each of the three research programs, of which we have achieved one milestone of \$2.5 million in one program, and additional, reduced research and regulatory milestones for subsequent products. We also are eligible to receive future commercial sales milestones of \$75 million based on certain specified thresholds of aggregate, worldwide net sales of all engineered T cell products within each of the three research programs. Further, we are eligible to receive tiered royalties of low double-digit percentages of Juno Therapeutics' net sales of products licensed under our collaboration agreement. Juno Therapeutics' obligation to pay royalties on a licensed product will expire on a product-by-product and country-by-country basis upon the later of the tenth anniversary of the first commercial sale of such licensed product and the expiration of the last to expire valid claim within the licensed patents covering such licensed product. If Juno Therapeutics is required to pay royalties on net sales of a licensed product to a third party because the licensed product is covered under the third party's patent, then Juno Therapeutics can credit a certain percentage of its payments to the third party against the royalties it owes us, subject to certain maximum deduction limits.

We will own any inventions developed by our employees and agents during our collaboration with Juno Therapeutics. Juno Therapeutics and we will jointly own any inventions made jointly by employees or agents of Juno Therapeutics and us during our collaboration with Juno Therapeutics. We retain control, at our own cost, of the prosecution and maintenance of our solely owned patents. Juno Therapeutics and we will be jointly responsible for the prosecution and maintenance of any jointly owned patents. We hold the final decision making authority with respect to claims of jointly owned patents relating to our genome editing technology and Juno Therapeutics holds the final decision making authority with respect to claims of jointly owned patents relating to CAR and TCR engineered T cell products.

Unless terminated earlier, the term of the collaboration agreement will expire on a product-by-product and country-by-country basis until the date no further payments are due to us from Juno Therapeutics. Juno Therapeutics may terminate the agreement for convenience in its entirety upon six months' written notice to us. Either Juno Therapeutics or we may terminate the agreement if the other party is in material breach and fails to cure such breach within the specified cure period. Either Juno Therapeutics or we may terminate the agreement in the event of insolvency or bankruptcy of the other party.

If Juno Therapeutics terminates the agreement as a result of our uncured material breach, Juno Therapeutics' rights and licenses to our specified patent rights, Juno Therapeutics' obligations to pay us certain research milestones and royalties, and Juno Therapeutics' rights to prosecute, maintain, and enforce certain patent rights each continue as set forth under the agreement. If Juno Therapeutics terminates the agreement for convenience or we terminate the agreement as a result of Juno Therapeutics' uncured material breach, the licenses we granted to Juno Therapeutics will terminate.

## Competition

The biotechnology and pharmaceutical industries, including in the gene therapy and genome-editing fields, are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on intellectual property and proprietary products. While we believe that our technology, development experience, and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical, and biotechnology companies, academic institutions and governmental agencies, and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

We compete in the segments of the pharmaceutical, biotechnology, and other related markets that utilize technologies encompassing genomic medicines to create therapies, including genome editing and gene therapy. There are additional companies that are working to develop therapies in areas related to our research programs.

Our platform and product focus is the development of therapies using CRISPR technology. Other companies developing CRISPR technology include Caribou Biosciences, CRISPR Therapeutics, ERS Genomics, Intellia Therapeutics, and TRACR Hematology. In addition, there have been and may continue to be discoveries of new CRISPR-based gene editing technologies.

There are additional companies developing therapies using additional genome editing technologies, including TALENs, meganucleases, Mega-TALs, and zinc finger nucleases. Potential advantages of these additional genome editing technologies include their degree of scientific characterization to date, which may allow for more rapid development of subsequent programs; the range of sites that each is able to recognize and the location of the DNA cut relative to the recognition sequence, each of which may allow for a different range of targets to be addressed; and the orientation of the DNA ends that are left behind after cutting. The companies developing these additional genome editing technologies include bluebird bio, Cellectis, Poseida Therapeutics, Precision Biosciences, and Sangamo Therapeutics. Additional companies developing gene therapy products include Abeona Therapeutics, Adverum Biotechnologies, AGTC Therapeutics, Dimension Therapeutics, REGENXBIO, Spark Therapeutics, uniQure, and Voyager Therapeutics. In addition to competition from other genome editing therapies or gene therapies, any products that we develop may also face competition from other types of therapies, such as small molecule, antibody, protein, oligonucleotide, or ribonucleic acid therapies.

Caribou Biosciences, CRISPR Therapeutics, and Intellia Therapeutics have all reported that they have obtained licenses to a family of patent applications that was filed by the University of California, the University of Vienna, and Emmanuelle Charpentier and has an earliest priority date which pre-dates the priority dates of our in-licensed patents and patent applications. CRISPR Therapeutics has reported that it has an exclusive license to patent rights from Emmanuelle Charpentier. Caribou Biosciences has reported that it has an exclusive license to patent rights from the University of California and the University of Vienna. Intellia Therapeutics has reported that it has an exclusive license to such rights from Caribou Biosciences in certain fields. The University of California derives rights in such applications from an assignment by Dr. Jennifer Doudna and certain other inventors listed on such applications. Dr. Doudna is a founder of Caribou Biosciences and has been publicly identified as an advisor to Intellia Therapeutics. For more information regarding the risks associated with third party intellectual property, please see “Risk Factors—Risks Related to Our Intellectual Property.”

In addition, many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology, and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products



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that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our programs are likely to be their efficacy, safety, convenience, and availability of reimbursement.

If our current programs are approved for the indications for which we are currently planning clinical trials, they may compete with other products currently under development, including genome editing and gene therapy products. Competition with other related products currently under development may include competition for clinical trial sites, patient recruitment, and product sales.

### **Intellectual Property**

Our success depends in part on our ability to obtain and maintain proprietary protection for our platform technology, programs, and know-how related to our business, defend and enforce our intellectual property rights, in particular, our patent rights, preserve the confidentiality of our trade secrets, and operate without infringing valid and enforceable intellectual property rights of others. We seek to protect our proprietary position by, among other things, exclusively licensing and filing U.S. and certain foreign patent applications related to our platform technology, existing and planned programs, and improvements that are important to the development of our business, where patent protection is available. We also rely on trade secrets, know-how, continuing technological innovation, and confidential information to develop and maintain our proprietary position and protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Our in-licensed patents and patent applications cover various aspects of our genome editing platform technology, including CRISPR systems that employ Cas9 including Cas9 nickases, *S. aureus* Cas9, high-fidelity Cas9 nucleases and Cas9 PAM variants, self-inactivating forms of Cas9, CRISPR systems that employ Cpf1 including Cpf1 nickases and other variants and self-inactivating forms of Cpf1, and also CRISPR systems that employ viral vectors for delivery, single guide RNAs, or modified guide RNAs. We also have filed patent applications and have in-licensed rights to filed patent applications directed to each of the four components of our genome editing platform technology. We intend to pursue, when possible, additional patent protection, including composition of matter, method of use, and process claims, directed to each component of our platform technology. We also intend to obtain rights to existing delivery technologies through one or more licenses from third parties.

Notwithstanding these efforts, we cannot be sure that patents will be granted with respect to any patent applications we have licensed or filed or may license or file in the future, and we cannot be sure that any patents we have licensed or patents that may be licensed or granted to us in the future will not be challenged, invalidated, or circumvented or that such patents will be commercially useful in protecting our technology. Moreover, trade secrets can be difficult to protect. While we have confidence in the measures we take to protect and preserve our trade secrets, such measures can be breached, and we may not have adequate remedies for any such breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. For more information regarding the risks related to our intellectual property, please see “Risk Factors—Risks Related to Our Intellectual Property.”

As of December 31, 2016, we owned ten pending U.S. non-provisional patent applications, nine pending European patent applications, 18 pending U.S. provisional patent applications, 12 pending Patent Cooperation Treaty, or PCT, applications, and other related patent applications in jurisdictions outside the United States and Europe, which include claims to compositions of matter and methods of use. One of these pending U.S. non-provisional applications and its foreign counterpart applications are co-owned with Broad and the University of Iowa Research Foundation, or Iowa, and we have obtained an exclusive license to such co-ownership rights from these third parties in the field of prevention or treatment of human disease using gene therapy or genome editing. In addition, four of these pending U.S. provisional patent applications are co-owned with certain of our collaborators because they encompass inventions developed under our collaborations. We intend to pursue, when possible, composition of matter, method of use, dosing, and formulation patent protection for genome editing products that we develop during the course of our business.



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As of December 31, 2016, we in-licensed 33 U.S. patents, which include claims to compositions of matter, methods of use, and certain processes as well as approximately 94 pending U.S. non-provisional patent applications, nine European patents and related validations, 53 pending European patent applications, four pending U.S. provisional patent applications, 13 pending PCT applications, and other related patent applications in jurisdictions outside the United States and Europe, which include claims to compositions of matter, methods of use, and certain processes. The patents and patent applications outside of the United States and Europe are held primarily in Canada, Japan, and Australia, although some of our in-licensed patent families were filed in a larger number of countries. Our in-licensed patents and patent applications claim the inventions of investigators at Broad, Harvard, MIT, MGH, The Rockefeller University, or Rockefeller, Duke University, or Duke, the University of Tokyo, or Tokyo, and Wageningen University, or Wageningen, and the majority of these licensed patents and patent applications are licensed on an exclusive basis. The exclusive licenses are, in some cases, limited to certain technical fields. Certain U.S. patent applications licensed to us by Broad include Tokyo and the National Institute of Health, or NIH, as joint applicants. Broad has only granted a license to us with respect to its interests and to Tokyo's interests in these U.S. patent applications but not to any foreign equivalents thereof. Broad does not and does not purport to grant any rights in NIH's interest in these U.S. patent applications under our agreement. As a result, we may not have exclusive rights under any U.S. patents that issue from these U.S. patent applications and we may not have any rights under any foreign patents that issue from any foreign equivalents thereof. For more information regarding these license agreements, please see the section of this Annual Report on Form 10-K titled "Business—License Agreements."

On January 11, 2016, the Patent Trial and Appeal Board of the USPTO, or PTAB, declared an interference between a pending U.S. patent application (U.S. Serial No. 13/842,859) that is owned by the University of California, the University of Vienna, and Emmanuelle Charpentier and 12 U.S. patents (U.S. Patent Nos. 8,697,359; 8,771,945; 8,795,965; 8,865,406; 8,871,445; 8,889,356; 8,895,308; 8,906,616; 8,932,814; 8,945,839; 8,993,233; and 8,999,641) that are co-owned by Broad and MIT, and in some cases Harvard, and in-licensed by us. On March 17, 2016, the PTAB re-declared the interference to add a pending U.S. patent application (U.S. Serial No. 14/704,551) that is co-owned by Broad, MIT, and Harvard, and in-licensed by us. An interference is a proceeding within the USPTO to determine priority of invention of the subject matter of patent claims filed by different parties. In the interference, the University of California, the University of Vienna, and Emmanuelle Charpentier asserted that inventors from the University of California and the University of Vienna, and Emmanuelle Charpentier made certain inventions claimed in the Broad, MIT and Harvard patents before the inventors from Broad, MIT and Harvard. The declaration of interference defined the invention that was subject to the declaration of interference, also referred to as "the count," as related to a method that involves contacting a target DNA in a eukaryotic cell with certain defined CRISPR/Cas9 components for the purpose of cleaving or editing a target DNA molecule or modulating transcription of at least one gene encoded thereon. All of the claims in the pending U.S. patent application that is owned by the University of California, the University of Vienna, and Emmanuelle Charpentier and all of the claims in the 12 U.S. patents and one pending U.S. patent application that are co-owned by Broad and MIT, and in some cases, Harvard, and in-licensed by us were implicated in the interference.

On February 15, 2017, the PTAB held that there is no interference-in-fact between the parties for the subject matter of the count. A judgment of no interference-in-fact means that no interference is needed to resolve priority between the parties because the PTAB determined that our in-licensed claims are directed to subject matter that is patentably distinct from those of the University of California, the University of Vienna, and Emmanuelle Charpentier. The interference proceeding has therefore ended. Therefore, the 12 U.S. patents and one U.S. patent application that we have in-licensed from Broad, acting on behalf of itself, MIT, and Harvard, as well as the U.S. patent application owned by the University of California, the University of Vienna, and Emmanuelle Charpentier, with respect to which the PTAB had declared an interference were not modified or revoked as a result of this interference proceeding. However, the University of California, the University of Vienna, and Emmanuelle Charpentier may request a rehearing of the judgment by the PTAB within 30 days and/or may appeal to the Court of Appeals for the Federal Circuit, or the Federal Circuit, within 63 days. It is uncertain when and in what manner the PTAB or Federal Circuit would act on such a request for rehearing or appeal. A final, non-appealable judgment of no interference-in-fact bars any further interference between the same parties for claims to the same invention as the count of the interference. However, as discussed below, certain of these 12 U.S. patents and one U.S. patent application are or may in the future be, subject to further intellectual property proceedings and disputes, including interference proceedings.

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Separately, ToolGen filed Suggestions of Interference in the USPTO on April 13, 2015, which became publicly available on November 12, 2015 and December 3, 2015, suggesting that it believes some of the claims pending in its applications (U.S. Serial No. 14/685,568 and U.S. Serial No. 14/685,510, respectively) interfere with certain claims in five U.S. patents, which we have in-licensed from Broad, acting on behalf of itself, MIT, and Harvard. These five U.S. patents are among the 12 U.S. patents with respect to which the PTAB had declared an interference with the pending U.S. patent application (U.S. Serial No. 13/842, 859) that is owned by the University of California, the University of Vienna, and Emmanuelle Charpentier. The Suggestions of Interference that were filed by ToolGen are still pending, and it is uncertain when and in what manner the USPTO will act on them.

A request for *ex parte* re-examination was filed with the USPTO on February 16, 2016 against one patent that we have in-licensed from Broad, acting on behalf of itself and MIT (U.S. Patent No. 8,771,945), which was subject to the interference proceeding involving the University of California, the University of Vienna, and Emmanuelle Charpentier and referenced in the Suggestions of Interference filed by ToolGen. *Ex parte* re-examination is a procedure through which a third party can anonymously request the USPTO to re-examine a granted patent because the third party believes the granted patent may not be patentable over prior art in the form of a printed publication or another patent. Before the USPTO will re-examine a granted patent, the third party requestor must establish that the submitted prior art establishes a substantial and new question of patentability. If the USPTO determines there is a substantial and new question of patentability, it grants the re-examination request and re-examines the patent after giving the patent owner the option of filing an initial statement. The request for *ex parte* re-examination of U.S. Patent No. 8,771,945 was granted on May 9, 2016 thereby initiating a re-examination procedure between the USPTO and Broad, acting on behalf of itself and MIT. The third party requestor does not participate in the re-examination procedure after filing the request except that it has the option of responding if the patent owner chooses to file an initial statement. On May 12, 2016, the PTAB suspended the re-examination of U.S. Patent No. 8,771,945 noting that it has jurisdiction over any file that involves a patent involved in the interference. It is uncertain when the PTAB will lift the suspension, however the PTAB may do so in light of the PTAB's no interference-in-fact holding. If Broad is unsuccessful during the re-examination, U.S. Patent No. 8,771,945 may be revoked or narrowed.

The 12 in-licensed U.S. patents and one in-licensed U.S. patent application that were the subject of the interference with the pending U.S. patent application (U.S. Serial No. 13/842,859) that is owned by the University of California, the University of Vienna, and Emmanuelle Charpentier (which includes the five in-licensed U.S. patents that are the subject of the Suggestions of Interference filed by ToolGen and the one in-licensed U.S. patent that is the subject of the request for *ex parte* re-examination) relate generally to the CRISPR/Cas9 system and its use in eukaryotic cells. The claims of the 12 in-licensed U.S. patents and one in-licensed U.S. patent application vary in scope and coverage and include claims that are directed to CRISPR/Cas9 systems that employ viral vectors for delivery, single guide RNAs, modified guide RNAs, *S. aureus* Cas9, or a Cas9 nickase and are relevant to our genome editing platform technology. The loss or narrowing in scope of one or more of these in-licensed patents could have a material adverse effect on the conduct of our business.

In addition, we or our licensors may be subject to claims that former employees, collaborators, or other third parties have an interest in our owned or in-licensed patents, patent applications, or other intellectual property as an inventor or co-inventor. If we are unable to obtain an exclusive license to any such third party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors. In addition, we may need the cooperation of any such co-owners to enforce such patents against third parties, and such cooperation may not be provided to us.

We or our licensors are subject to and may also become a party to similar proceedings or priority disputes in Europe or other foreign jurisdictions. The European Patent Office Opposition Division has initiated opposition proceedings in the European Patent Office, or EPO, against four European patents that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard (European Patent Nos. EP 2,771,468 B1, EP 2,784,162 B1, EP 2,896,697 B1 and EP 2,931,898 B1) and one European patent that we have in-licensed from Broad, acting on behalf of itself and MIT (European Patent No. EP 2,764,103 B1). The EPO opposition proceedings may involve issues including, but not limited to, procedural formalities related to filing the European patent application, priority, and the patentability of the involved claims. One or more of the third parties that have filed oppositions against European Patent Nos. EP 2,771,468 B1, EP 2,784,162 B1, EP 2,764,103 B1, EP 2,896,697 B1, and/or EP 2,931,898 or other third parties may file future oppositions

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against other European patents that we in-license or own. For example, we are aware that oppositions have been filed against two other European patents that we in-license from Broad, acting on behalf of itself, MIT and Harvard (European Patent Nos. EP 2,898,075 B1 and EP 2,921,557 B1). The deadline for filing oppositions against the second of these European patents is April 13, 2017. There may be other oppositions against this European patent that have not yet been filed or that have not yet been made available to the public. The loss of priority for, or the loss of, these European patents could have a material adverse effect on the conduct of our business.

For more information regarding the risks associated with the interference, the Suggestions of Interference, the request for *ex parte* re-examination, the European oppositions, and other potential third party intellectual property related disputes, please see “Risk Factors—Risks Related to Our Intellectual Property.”

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the United States, a patent’s term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. The Drug Price Competition and Patent Term Restoration Act of 1984 extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be extended and only those claims covering the approved drug or a method for using it may be extended.

### *CRISPR*

As of December 31, 2016, we owned ten pending U.S. non-provisional patent applications, nine pending European patent applications, 18 pending U.S. provisional patent applications, 12 pending PCT patent applications, and other related patent applications in jurisdictions outside the United States and Europe that are related to our CRISPR technology and which include claims directed to our genome editing platform, including our directed editing component, as well as composition of matter and method of use claims for our therapeutic programs, including LCA10 and other genetic and infectious eye disorders, and engineered T cells. One of these pending U.S. non-provisional applications and its foreign counterpart applications is co-owned with Broad and Iowa and we have obtained an exclusive license to such co-ownership rights from these third parties in the field of prevention or treatment of human disease using gene therapy or genome editing. In addition, four of these pending U.S. provisional patent applications are co-owned with certain of our collaborators because they encompass inventions developed under our collaborations. If issued as U.S. patents, and if the appropriate maintenance fees are paid, the U.S. patent applications would be expected to expire between 2034 and 2037, excluding any additional term for patent term adjustments or patent term extensions.

As of December 31, 2016, we in-licensed 26 U.S. patents, eight European patents and related validations, and over 450 pending patent applications, including approximately 82 pending U.S. non-provisional patent applications, 44 pending European patent applications, four pending U.S. provisional patent applications, 13 pending PCT patent applications, and other related patent applications in jurisdictions outside the United States and Europe that are related to our CRISPR technology collectively from Broad, Harvard, MIT, MGH, Duke, Iowa, Tokyo, and Wageningen, as more fully described below. The claims from our in-licensed portfolio include claims to compositions of matter, methods of use, and certain processes. These include claims directed to CRISPR systems that employ Cas9 including Cas9 nickases, *S. aureus* Cas9, high-fidelity Cas9 nucleases, Cas9 PAM variants and self-inactivating forms of Cas9, CRISPR systems that employ Cpf1 including Cpf1 nickases and other variants and self-inactivating forms of Cpf1, and also CRISPR systems that employ viral vectors for delivery, single guide RNAs, or modified guide RNAs. Our current in-licensed U.S. patents, if the appropriate maintenance fees are paid, are expected to expire between 2033 and 2036, excluding any additional term for patent term adjustments or patent term extensions.

### *LCA10*

As of December 31, 2016, we owned one pending U.S. non-provisional patent application, one pending European patent application, one pending Canadian patent application, and one pending U.S. provisional patent application which are directed to compositions of matter, including guide RNAs directed to CEP290, and methods of use

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for the treatment of LCA10. If issued as a U.S. patent, and if the appropriate maintenance fees are paid, the U.S. patent application would be expected to expire between 2035 and 2037, excluding any additional term for patent term adjustments or patent term extensions.

### *Trademarks*

As of December 31, 2016, our registered trademark portfolio consisted of two registered trademarks and one pending trademark application in the United States for the mark EDITAS and one corresponding registered trademark in each of Australia, China, Europe, Japan, and Switzerland.

### **License Agreements**

We are a party to a number of license agreements under which we license patents, patent applications, and other intellectual property from third parties. The licensed intellectual property covers, in part, CRISPR and transcription activator-like effector (TALE)-related compositions of matter and their use for genome editing. These licenses impose various diligence and financial payment obligations on us. We expect to continue to enter into these types of license agreements in the future. We consider the following license agreements to be material to our business.

#### *The Broad Institute and President and Fellows of Harvard College License Agreement*

In October 2014, we entered into a license agreement with Broad and Harvard, for specified patent rights. In December 2016, we amended and restated this license agreement and further amended the agreement in March 2017. We refer to such amended and restated agreement, as amended, as the Cas9-I License Agreement. Among other things, the Cas9-I License Agreement amended the original license agreement by excluding additional fields from the scope of the exclusive license granted to us; converting the exclusive license to three specified targets to a non-exclusive license, subject to specified limitations; revising certain provisions relating to the rights of Harvard and Broad to grant further licenses under specified circumstances to third parties that wish to develop and commercialize products that target a particular gene and that otherwise would fall within the scope of our exclusive license; and providing Harvard and Broad with certain rights to designate, and reserve all rights to, gene targets for which the designating institution has an interest in researching and developing products that would otherwise be covered by rights licensed to us. The licenses granted to us under the Cas9-I License Agreement include rights to certain patents solely owned by Harvard, which we refer to as Harvard Cas9-I Patent Rights, certain patents co-owned by MIT and Broad, certain patents co-owned by MIT, Rockefeller, and Broad, and certain patents co-owned by MIT, Broad and Harvard. We refer to all the patents and patent applications licensed to us under the Cas9-I License Agreement as the Harvard/Broad Cas9-I Patent Rights.

Certain patent applications in the Harvard/Broad Cas9-I Patent Rights are jointly owned by Rockefeller. In February 2017, Broad and Rockefeller entered into an inter-institutional agreement pursuant to which Rockefeller authorized Broad to act as its sole and exclusive agent for the purposes of licensing Rockefeller's rights in such Harvard/Broad Cas9-I Patent Rights and any additional related patents or patent applications that Rockefeller may jointly own with Broad. In March 2017, we further amended the Cas9-I License Agreement to include a license to Rockefeller's rights in such patents and patent applications.

The Harvard/Broad Cas9-I Patent Rights are directed, in part, to certain CRISPR/Cas9 and TALE-related compositions of matter and their use for genome editing and to certain CRISPR/Cas9 and TALE-related delivery technologies. Pursuant to the Cas9-I License Agreement, and as of December 31, 2016, we have certain rights under 32 U.S. patents, 66 pending U.S. patent applications, nine European patents and related validations, 35 pending European patent applications, two pending PCT applications, and other related patent applications in jurisdictions outside of the United States and Europe.

Pursuant to the Cas9-I License Agreement, Harvard and Broad granted us an exclusive, worldwide, royalty-bearing, sublicensable license to the Harvard/Broad Cas9-I Patent Rights to make, have made, use, sell, offer for sale, have sold, import, and export products and services in the field of the prevention and treatment of human disease, subject to certain limitations and retained rights. The exclusive license granted by Broad and Harvard excludes certain fields, including the modification of animals or animal cells for the creation and sale of organs suitable for

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xenotransplantation into humans; the research, development and commercialization of products or services in the field of livestock applications; plant-based agricultural products; and, subject to certain limitations, products providing nutritional benefits. Moreover, the license granted by Broad is non-exclusive with respect to the treatment of medullary cystic kidney disease 1 and three other specified targets, subject to the limitation that for such three targets, each of Broad and Harvard is only permitted to grant a non-exclusive license to one third party at a time with respect to each such target within the field of exclusive license granted to us. Harvard and Broad also granted us a non-exclusive, worldwide, royalty-bearing, sublicensable license to the Harvard/Broad Cas9-I Patent Rights for all purposes, with the exception that the non-exclusive license to certain Harvard Cas9-I Patent Rights excludes the modification of animals or animal cells for the creation and sale of organs suitable for xenotransplantation into humans and the development and commercialization of products or services in the field of livestock applications. In addition to the exclusions described above, the following are excluded from the scope of both the exclusive and non-exclusive licenses granted to us under the Cas9-I License Agreement: human germline modification; the stimulation of biased inheritance of particular genes or traits within a population of plants or animals; the research, development, manufacturing, or commercialization of sterile seeds; and the modification of the tobacco plant with specified exceptions.

We are obligated to use commercially reasonable efforts to research, develop, and commercialize products for the prevention or treatment of human disease under the Cas9-I License Agreement. Also, we are required to achieve certain development milestones within specified time periods for products incorporating the CRISPR/Cas9, TAL, and delivery-related technologies covered by the Harvard/Broad Cas9-I Patent Rights. Harvard and Broad have the right to terminate our license with respect to the Harvard/Broad Cas9-I Patent Rights covering the technology or technologies with respect to which we fail to achieve these development milestones.

The licenses granted by Broad and Harvard to us under the Cas9-I License Agreement are subject to retained rights of the U.S. government in the Harvard/Broad Cas9-I Patent Rights and the rights retained by Broad, Harvard, MIT, and Rockefeller on behalf of themselves and other academic, government and non-profit entities, to practice the Harvard/Broad Cas9-I Patent Rights for research, educational, or teaching purposes. In addition, certain rights granted to us under the Cas9-I License Agreement are further subject to a non-exclusive license to the Howard Hughes Medical Institute for research purposes. Our exclusive license rights also are subject to rights retained by Broad, Harvard, MIT, and Rockefeller any third party to research, develop, make, have made, use, offer for sale, sell, have sold, import or otherwise exploit the Harvard/Broad Cas9-I Patent Rights and licensed products as research products or research tools, or for research purposes.

We have the right to sublicense our licensed rights provided that the sublicense agreement must be in compliance and consistent with the terms of the Cas9-I License Agreement. Any sublicense agreement cannot include the right to grant further sublicenses without the written consent of Broad and Harvard. In addition, any sublicense agreements must contain certain terms, including a provision requiring the sublicensee to indemnify Harvard, Broad, MIT, and Howard Hughes Medical Institute according to the same terms as are provided in the Cas9-I License Agreement and a statement that Broad, Harvard, MIT, and Howard Hughes Medical Institute are intended third party beneficiaries of the sublicense agreement for certain purposes.

Under the agreement, Harvard and Broad also retained rights to grant further licenses under specified circumstances to third parties, other than specified entities, that wish to develop and commercialize products that target a particular gene and that otherwise would fall within the scope of our exclusive license from Harvard and Broad. If a third party requests a license under the Harvard/Broad Cas9-I Patent Rights for the development and commercialization of a product that would be subject to our exclusive license grant from Harvard and Broad under the Cas9-I License Agreement, Harvard and Broad may notify us of the request. We refer to these requests as Cas9-I Third Party Proposed Product Requests. A Cas9-I Third Party Proposed Product Request must be accompanied by a research, development and commercialization plan reasonably satisfactory to Harvard and Broad, including evidence that the third party has, or reasonably expects to have, access to any necessary intellectual property and funding. Harvard and Broad may not grant a Cas9-I Third Party Proposed Product Request (i) if we, directly or through any of our affiliates, sublicensees, or collaborators are researching, developing, or commercializing a product directed to the same gene target that is the subject of the Cas9-I Third Party Proposed Product Request, or Cas9-I Licensee Product, and we can demonstrate such ongoing efforts to Harvard's and Broad's reasonable satisfaction, or (ii) if we, directly or through any of our affiliates or sublicensees, wish to do so either alone or with a collaboration partner, and we can demonstrate to Harvard and Broad's

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reasonable satisfaction that we are interested in researching, developing, and commercializing the Cas9-I Licensee Product, that we have a commercially reasonable research, development, and commercialization plan to do so, and we commence and continue reasonable commercial efforts under such plan. If we, directly or through any of our affiliates, sublicensees, or collaborators, are not researching, developing, or commercializing a Cas9-I Licensee Product nor able to develop and implement a plan reasonably satisfactory to Harvard and Broad, Harvard and Broad may grant an exclusive or non-exclusive license to the third party on a gene target-by-gene target basis. Beginning in December 2018, our process to address Cas9-I Third Party Proposed Product Requests will conform to the process established in our Cpfl License Agreement described below.

The Cas9-I License Agreement also provides Broad with the right, after a specified period of time and subject to certain limitations, to designate gene targets for which Broad, whether alone or together with an affiliate or third party, has an interest in researching and developing products that would otherwise be covered by rights licensed to us under the Cas9-I License Agreement. Broad may not so designate any gene target for which we, directly or through any of our affiliates, sublicensees, or collaborators, are researching, developing, or commercializing a product, or for which we can demonstrate to Broad's reasonable satisfaction that we are interested in researching, developing, and commercializing a product, that we have a commercially reasonable research, development, and commercialization plan to do so, and we commence and continue reasonable commercial efforts under such plan. If we directly or through any of our affiliates, sublicensees, or collaborators, are not researching, developing, or commercializing a product directed toward the gene target designated by Broad and are not able to develop and implement a plan reasonably satisfactory to Broad, Broad is entitled to reserve all rights under the Cas9-I License Agreement, including the right to grant exclusive or non-exclusive licenses to third parties, to develop and commercialize products directed to such gene target and our license granted with respect to such gene target will terminate, and we will not be entitled under the Cas9-I License Agreement to develop and commercialize products directed to that gene target.

Under the Cas9-I License Agreement, we paid Broad and Harvard an upfront license fee in the low six figures and issued a single-digit percentage of shares of our common stock to Broad (with Broad holding a right to request re-issuance to its designees, including MIT or MIT's designee) and Harvard. We also must pay an annual license maintenance fee ranging from the low- to mid-five figures to the low-six figures, depending on the calendar year. This annual license maintenance fee is creditable against royalties owed on licensed products and services in the same year as the maintenance fee is paid. We are obligated to reimburse Broad and Harvard for expenses associated with the prosecution and maintenance of the Harvard/Broad Cas9-I Patent Rights, including expenses associated with any interference proceedings in the USPTO, any opposition proceedings in the EPO, or any other *inter partes* or other post grant proceedings in these or other jurisdictions where we are seeking patent protection. Therefore, we are obligated to reimburse Broad and/or Harvard for expenses associated with the interference and opposition proceedings involving patents licensed to us under this agreement (described in more detail under "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K).

Broad and Harvard are collectively entitled to receive clinical and regulatory milestone payments totaling up to \$14.8 million in the aggregate per licensed product approved in the United States, the European Union and Japan for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. If we undergo a change of control during the term of the Cas9-I License Agreement, these clinical and regulatory milestone payments will be increased by a certain percentage in the mid double-digits. We are also obligated to make additional payments to Broad and Harvard, collectively, of up to an aggregate of \$54.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. Broad and Harvard are collectively entitled to receive clinical and regulatory milestone payments totaling up to \$4.1 million in the aggregate per licensed product approved in the United States and at least one jurisdiction outside the United States for the prevention or treatment of a human disease that afflicts fewer than a specified number of patients in the aggregate in the United States or a specified number of patients per year in the United States, which we refer to as an ultra-orphan disease. We are also obligated to make additional payments to Broad and Harvard, collectively, of up to an aggregate of \$36.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or treatment of an ultra-orphan disease.

Broad and Harvard, collectively, are entitled to receive mid single-digit percentage royalties on net sales of licensed products for the prevention or treatment of human disease, and ranging from low single-digit to high



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single-digit percentage royalties on net sales of other licensed products and services, made by us, our affiliates, or our sublicensees. The royalty percentage depends on the licensed product and licensed service, and whether such licensed product or licensed service is covered by a valid claim within the Harvard/Broad Cas9-I Patent Rights. If we are legally required to pay royalties to a third party on net sales of our licensed products because such third party holds patent rights that cover such licensed product, then we can credit up to a mid double-digit percentage of the amount paid to such third party against the royalties due to Harvard and Broad in the same period. Our obligation to pay royalties will expire on a product-by-product and country-by-country basis upon the later of the expiration of the last to expire valid claim of the Harvard/Broad Cas9-I Patent Rights that cover the composition, manufacture, or use of each covered product or service in each country or the tenth anniversary of the date of the first commercial sale of the licensed product or licensed service. If we sublicense any of the Harvard/Broad Cas9-I Patent Rights to a third party pursuant to our exclusive license under the Cas9-I License Agreement, Broad and Harvard, collectively, have the right to receive a low double-digit percentage of the sublicense income, which percentage decreases to a high single-digit percentage for licensed products for the prevention or treatment of human disease under sublicenses executed after we meet certain clinical milestones.

Broad and Harvard retain control of the prosecution of their respective patent rights. If an interference is declared or a derivation proceeding is initiated, with respect to any Harvard/Broad Cas9-I Patent Rights, then our prosecution related rights, including our right to receive correspondence from a patent office, will be suspended with respect to the patent rights involved in the interference or derivation proceeding until, under some circumstances, we enter into a common interest agreement with that institution. Nevertheless, we remain responsible for the cost of such interference or derivation proceeding. On January 11, 2016, the PTAB declared an interference between a pending U.S. patent application (U.S. Serial No. 13/842,859) that is owned by the University of California, the University of Vienna, and Emmanuelle Charpentier and 12 U.S. patents (U.S. Patent Nos. 8,697,359; 8,771,945; 8,795,965; 8,865,406; 8,871,445; 8,889,356; 8,895,308; 8,906,616; 8,932,814; 8,945,839; 8,993,233; and 8,999,641) that are co-owned by Broad and MIT, and in some cases Harvard, and in-licensed by us under the Cas9-I License Agreement. On March 17, 2016, the PTAB re-declared the interference to add a pending U.S. patent application (U.S. Serial No. 14/704,551) that is co-owned by Broad, MIT, and Harvard, and also in-licensed by us under the Cas9-I License Agreement. On February 15, 2017, the PTAB held that there is no interference-in-fact and the interference proceeding has therefore ended. However, the University of California, the University of Vienna, and Emmanuelle Charpentier may request a rehearing of the judgment by the PTAB and/or may appeal to the Federal Circuit. We are responsible for the cost of the interference proceeding with respect to these patents and this patent application. Broad and Harvard are required to maintain any application or patent within the Harvard/Broad Patents Rights so long as we meet our obligation to reimburse Broad and Harvard for expenses related to prosecution and there is a good faith basis for doing so. If we cease payment for the prosecution of any Harvard/Broad Patent Right, then any license granted to us with respect to such Harvard/Broad Patent Right will terminate.

We have the first right, but not the obligation, to enforce the Harvard/Broad Cas9-I Patent Rights with respect to our licensed products so long as certain conditions are met, such as providing Broad and Harvard with evidence demonstrating a good faith basis for bringing suit against a third party. We are solely responsible for the costs of any lawsuits we elect to initiate and cannot enter into a settlement without the prior written consent of Broad and Harvard (and MIT and Rockefeller, if applicable). Any sums recovered in such lawsuits will be shared between us, Broad, and Harvard.

Unless terminated earlier, the term of the Cas9-I License Agreement will expire on a country-by-country basis, upon the expiration of the last to expire valid claim of the Harvard/Broad Cas9-I Patent Rights in such country. However, our royalty obligations, discussed above, may survive expiration or termination. We have the right to terminate the agreement at will upon four months' written notice to Broad and Harvard. Broad and Harvard may terminate the agreement upon a specified period of notice in the event of our uncured material breach, such notice period varying depending on the nature of the breach. Both Broad and Harvard may terminate the Cas9-I License Agreement immediately if we challenge the enforceability, validity, or scope of any Harvard/Broad Patent Right or assist a third party to do so, or in the event of our bankruptcy or insolvency. Neither Broad nor Harvard acting alone has the right to terminate the Cas9-I License Agreement. However, Broad and Harvard may separately terminate the licenses granted to us with respect to their respective patent rights upon the occurrence of the same events that would give rise to the right of both institutions acting collectively to terminate the Cas9-I License Agreement.

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### *The Broad Institute—Cpfl License Agreement*

In December 2016, we entered into a license agreement, or the Cpfl License Agreement, with Broad, for specified patent rights, or Cpfl Patent Rights, related primarily to Cpfl compositions of matter and their use for gene editing. Pursuant to the Cpfl License Agreement, Broad, on behalf of itself, Harvard, MIT, Wageningen, and Tokyo, or collectively, the Cpfl Institutions, granted us an exclusive, worldwide, royalty-bearing, sublicensable license to the Cpfl Patent Rights, to make, have made, use, have used, sell, offer for sale, have sold, export and import products solely in the field of the prevention or treatment of human disease using gene therapy, editing of genetic material, or targeting of genetic material, subject to certain limitations and retained rights, or collectively, the Exclusive Cpfl Field, as well as a non-exclusive, worldwide, royalty-bearing, sublicensable license to the Cpfl Patent Rights for all other purposes, subject to certain limitations and retained rights. The licenses granted to us under the Cpfl License Agreement exclude certain fields, including human germline modification; the stimulation of biased inheritance of particular genes or traits within a population of plants or animals; the research, development, manufacturing, or commercialization of sterile seeds; and the modification of the tobacco plant with specified exceptions.

Tokyo and NIH are joint owners on certain Cpfl Patent Rights. Broad has only granted a license to us with respect to its interests and to Tokyo's interests in these U.S. patent applications but not to any foreign equivalents thereof. Broad does not, and does not purport to, grant any rights in NIH's interest in these U.S. patent applications under our agreement. As a result, we may not have exclusive rights under any U.S. patents that issue from these U.S. patent applications and we may not have any rights under any foreign patents that issue from any foreign equivalents thereof.

Pursuant to the Cpfl License Agreement, and as of December 31, 2016, we have certain rights under one pending U.S. patent application, one pending European patent application, four pending U.S. provisional patent applications, three pending PCT applications, and other related patent applications in jurisdictions outside of the United States and Europe.

We are obligated to use commercially reasonable efforts to research, develop, and commercialize licensed products in the Exclusive Cpfl Field. We are also required to achieve certain development milestones within specified time periods for products covered by the Cpfl Patent Rights, with Broad having the right to terminate the Cpfl License Agreement if we fail to achieve these milestones within the required time periods. We have the right to sublicense our licensed rights provided that the sublicense agreement must be in compliance and consistent with the terms of the Cpfl License Agreement. Any sublicense agreement cannot include the right to grant further sublicenses without the written consent of Broad. In addition, any sublicense agreements must contain certain terms, including a provision requiring the sublicensee to indemnify the Cpfl Institutions according to the same terms as are provided in the Cpfl License Agreement and a statement that the Cpfl Institutions are intended third party beneficiaries of the sublicense agreement for certain purposes.

The licenses granted to us under the Cpfl License Agreement are subject to retained rights of the U.S. government in the Cpfl Patent Rights and rights retained by the Cpfl Institutions on behalf of themselves and other academic, government and non-profit entities, to practice the Cpfl Patent Rights for research, teaching, or educational purposes. Our exclusive license rights also are subject to rights retained by the Cpfl Institutions for themselves and any third party to research, develop, make, have made, use, offer for sale, sell, have sold, import or otherwise exploit the Cpfl Patent Rights and licensed products as research products or research tools, or for research purposes.

Under the Cpfl License Agreement, Broad also retained rights to grant further licenses under specified circumstances to third parties that wish to develop and commercialize products that target a particular gene and that otherwise would fall within the scope of our exclusive license from Broad. Beginning in December 2018, if a third party requests a license under the Cpfl Patent Rights for the development and commercialization of a product that would be subject to our exclusive license grant from Broad, or Cpfl Third Party Proposed Product Request, Broad may notify us of such request. A Cpfl Third Party Proposed Product Request must be accompanied by a research, development and commercialization plan reasonably satisfactory to Broad, including evidence that the third party has, or reasonably expects to have, access to any necessary intellectual property and funding. Broad may not grant a Cpfl Third Party Proposed Product Request (i) if we, directly or through any of our affiliates, sublicensees, or collaborators are



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researching, developing, or commercializing a product directed to the same gene target that is the subject of the Cpfl Third Party Proposed Product Request, or Cpfl Licensee Product, and we can demonstrate such ongoing efforts to Broad's reasonable satisfaction, or (ii) if we, directly or through any of our affiliates or sublicensees, wish to do so either alone or with a collaboration partner, and we can demonstrate to Broad's reasonable satisfaction that we are interested in researching, developing, and commercializing a Cpfl Licensee Product, that we have a commercially reasonable research, development, and commercialization plan to do so, and we commence and continue reasonable commercial efforts under such plan. If we, directly or through any of our affiliates, sublicensees, or collaborators, are not researching, developing, or commercializing a Cpfl Licensee Product nor able to develop and implement a plan reasonably satisfactory to Broad, Broad may grant an exclusive or non-exclusive license to the third party on a gene target-by-gene target basis.

The Cpfl License Agreement also provides Broad with the right, beginning in December 2017 and subject to certain limitations, to designate gene targets for which Broad, whether alone or together with a Cpfl Institution, affiliate or third party, has an interest in researching and developing products that would otherwise be covered by rights licensed to us under the Cpfl License Agreement. Broad may not so designate any gene target for which we, directly or through any of our affiliates, sublicensees, or collaborators, are researching, developing, or commercializing a product, or for which we can demonstrate to Broad's reasonable satisfaction that we are interested in researching, developing, and commercializing a product, that we have a commercially reasonable research, development, and commercialization plan to do so, and we commence and continue reasonable commercial efforts under such plan. If we, directly or through any of our affiliates, sublicensees, or collaborators, are not researching, developing, or commercializing a product directed toward the gene target designated by Broad and are not able to develop and implement a plan reasonably satisfactory to Broad, Broad is entitled to reserve all rights under the Cpfl License Agreement, including the right to grant exclusive or non-exclusive licenses to third parties, to develop and commercialize products directed to such gene target, our license with respect to such gene target will terminate, and we will not be entitled under the Cpfl License Agreement to develop and commercialize products directed to such gene target.

Under the Cpfl License Agreement, we paid Broad and Wageningen an aggregate upfront license fee in the mid seven digits and issued to Broad and Wageningen promissory notes, or Initial Promissory Notes, in an aggregate principal amount of \$10.0 million. The Initial Promissory Notes bear interest at 4.8% per annum. Principal and interest on the Initial Promissory Notes will be payable on the first anniversary of the issuance date (or if earlier, a specified period of time following a sale of our company). We may elect to make any payment of amounts outstanding under the Initial Promissory Notes either in the form of cash or, subject to certain conditions, in shares of our common stock of equal value, with such shares being valued for such purpose at the closing price of our common stock as reported the NASDAQ Stock Market for the trading day immediately preceding the date of such payment if our common stock is then listed on the NASDAQ Stock Market. In the event of a change of control of our company or a sale of our company, we will be required to pay all remaining principal and accrued interest on the Initial Promissory Notes in cash within a specified period following such event.

Broad and Wageningen are collectively entitled to receive clinical and regulatory milestone payments totaling up to \$20.0 million in the aggregate per licensed product approved in the United States, the European Union and Japan for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. If we undergo a change of control during the term of the Cpfl License Agreement, certain of these clinical and regulatory milestone payments will be increased by a certain percentage in the mid double-digits. We are also obligated to make additional payments to Broad and Wageningen, collectively, of up to an aggregate of \$54.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. Broad and Wageningen are collectively entitled to receive clinical and regulatory milestone payments totaling up to \$6.0 million in the aggregate per licensed product approved in the United States, the European Union and Japan for the prevention or treatment of an ultra-orphan disease. We are also obligated to make additional payments to Broad and Wageningen, collectively, of up to an aggregate of \$36.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or treatment of an ultra-orphan disease.

Broad and Wageningen, collectively, are entitled to receive mid single-digit percentage royalties on net sales of products for the prevention or treatment of human disease, and ranging from sub single-digit to high single-digit

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percentage royalties on net sales of other products and services, made by us, our affiliates, or our sublicensees. The royalty percentage depends on the product and service, and whether such licensed product or licensed service is covered by a valid claim within the Cpfl Patent Rights. If we are legally required to pay royalties to a third party on net sales of our products because such third party holds patent rights that cover such licensed product, then we can credit up to a mid double-digit percentage of the amount paid to such third party against the royalties due to Broad and Wageningen in the same period. Our obligation to pay royalties will expire on a product-by-product and country-by-country basis upon the later of the expiration of the last to expire valid claim of the Cpfl Patent Rights that covers each licensed product or licensed service in each country or the tenth anniversary of the date of the first commercial sale of the product or service. If we sublicense any of the Cpfl Patent Rights to a third party, Broad and Wageningen, collectively, have the right to receive high single-digit to low double-digit percentages of the sublicense income, depending on the stage of development of the products or services in question at the time of the sublicense.

Under the Cpfl License Agreement, Broad and Wageningen are also entitled, collectively, to receive success payments in the event our market capitalization reaches specified thresholds ascending from a high nine digit dollar amount to \$10.0 billion, or Market Cap Success Payments, or sale of our company for consideration in excess of those thresholds, or Company Sale Success Payments, which collectively with the Market Cap Success Payments, are the Success Payments. The Success Payments that may be paid to Broad and Wageningen range from a mid seven digit dollar amount to a mid eight digit dollar amount, and collectively will not exceed, in aggregate, \$125.0 million, which maximum would be payable only if we achieve a market capitalization threshold of \$10.0 billion and have at least one product candidate covered by a claim of a patent right licensed to us under either the Cpfl License Agreement or the Cas9-I License Agreement that is or was the subject of a clinical trial pursuant to development efforts by us or any of our affiliates or sublicensees. Market Cap Success Payments are payable by us in cash or in the form of promissory notes on substantially the same terms and conditions as the Initial Promissory Notes, except that the maturity date of such notes will, subject to certain exceptions, be 150 days following issuance. Following a change in control of our company, Market Cap Success Payments are required to be made in cash. Company Sale Success Payments are payable solely in cash.

In addition, in the event that a sale of our company or change of control has occurred and the maximum amount of potential Success Payments under the Cpfl License Agreement has not been paid to Broad and Wageningen, Broad and Wageningen are entitled to receive, upon the subsequent achievement of specified regulatory milestones, percentages ranging from high single digits to mid-to-low double digits of the remaining unpaid maximum amount of Success Payments. Broad and Wageningen are further entitled to receive up to the full remaining unpaid maximum amount of Success Payments upon the subsequent achievement of specified sales milestones. All such post-sale or post-change of control milestone payments are required to be made in cash.

Broad retains control of the prosecution and maintenance of the Cpfl Patent Rights. We have the right to provide input in the prosecution of the Cpfl Patent Rights, including to direct Broad to file and prosecute patents in certain countries. We are also obligated to reimburse Broad and Wageningen for all unreimbursed expenses incurred by them in connection with the prosecution and maintenance of the Cpfl Patent Rights prior to the date of the Cpfl License Agreement, and to reimburse Broad for expenses associated with the prosecution and maintenance of the Cpfl Patent Rights following the date of the Cpfl License Agreement.

We have the first right, but not the obligation, to enforce the Cpfl Patent Rights with respect to our licensed products in the Exclusive Cpfl Field so long as certain conditions are met, such as providing Broad and the applicable Cpfl Institutions with evidence demonstrating a good faith basis for bringing suit against a third party. We are solely responsible for the costs of any lawsuits we elect to initiate and cannot enter into a settlement without the prior written consent of Broad. Any sums recovered in such lawsuits will be shared between Broad, Wageningen, and us.

Unless terminated earlier, the term of the Cpfl License Agreement will expire on a country-by-country basis, upon the expiration of the last to expire valid claim of the Cpfl Patent Rights in such country. However, our royalty obligations, discussed above, may survive expiration or termination. We have the right to terminate the Cpfl License Agreement at will upon four months' written notice to Broad. Either party may terminate the Cpfl License Agreement upon a specified period of notice in the event of the other party's uncured material breach of a material obligation, such notice period varying depending on the nature of the breach. Broad may terminate the Cpfl License Agreement

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immediately if we challenge the enforceability, validity, or scope of any Cpfl Patent Right or assist a third party to do so, or in the event of our bankruptcy or insolvency.

### *The Broad Institute—Cas9-II License Agreement*

In December 2016, we entered into a license agreement, or the Cas9-II License Agreement, with Broad for specified patent rights, or the Cas9-II Patent Rights, related primarily to certain Cas9 compositions of matter and their use for gene editing. Pursuant to the Cas9-II License Agreement, Broad, on behalf of itself, MIT, Harvard, and Iowa, or collectively, the Cas9-II Institutions, granted us an exclusive, worldwide, royalty-bearing sublicensable license to certain of the Cas9-II Patent Rights in the field of the prevention or treatment of human disease using gene therapy, editing of genetic material, or targeting of genetic material, subject to certain limitations and retained rights, as well as a non-exclusive, worldwide, royalty-bearing sublicensable license to all of the Cas9-II Patent Rights for all purposes, subject to certain limitations and retained rights, in each case on terms substantially similar to the licenses granted to us under Cpfl License Agreement, except that:

- the terms relating to retained rights of the Cas9-II Institutions to grant licenses to the Cas9-II Patent Rights under specified circumstances to third parties, including to third parties that wish to develop and commercialize products that target a particular gene and that otherwise would fall within the scope of our exclusive license are on terms substantially similar to those under the Cas9-I License Agreement;
- the upfront license fee is in the low seven digits and is payable in cash;
- we are required to pay an annual license maintenance fee in the mid-five figures;
- the clinical and regulatory milestone payments per licensed product approved in the United States, the European Union and Japan for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States total up to \$3.7 million in the aggregate, and the sales milestone payments for any such licensed product total up to \$13.5 million in the aggregate;
- we are required to pay clinical and regulatory milestone payments totaling up to \$1.1 million in the aggregate per licensed product approved in the United States and the European Union or Japan for the prevention or treatment of a human disease that afflicts fewer than a specified number of patients in the United States, plus sales milestone payments of up to \$9.0 million for any such licensed product;
- the royalty rate on net sales of licensed products for the prevention or treatment of human disease that are covered by the Cas9-II Patent Rights subject to our exclusive license is a low single-digit percentage, and the royalty rate on net sales of other licensed products and licensed services covered by the Cas9-II Patent Rights subject to our exclusive license ranges from sub single-digit to low single-digit percentages;
- the royalty rates for the sale of licensed products and licensed services covered by the Cas9-II Patent Rights subject only to our non-exclusive license are 50% of the applicable royalty rates for licensed products and licensed services covered by the Cas9-II Patent Rights subject to our exclusive license;
- the potential Success Payments are payable based on our market capitalization reaching specified thresholds ascending from a low ten digit dollar amount to \$9.0 billion or a sale of our company for consideration in excess of those thresholds, and will not exceed, in the aggregate, \$30.0 million, which maximum would be owed only if we reach a market capitalization threshold of \$9.0 billion and have at least one product candidate covered by a claim of a patent right licensed to us under either the Cas9-II License Agreement or the Cas9-I License Agreement that is or was the subject of a clinical trial pursuant to development efforts by us or any of our affiliates or sublicensees;
- many of our rights and obligations with respect to the control and enforcement of the Cas9-II Patent Rights, including our right to direct Broad to file and prosecute patents in certain countries, our obligation to

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reimburse Broad for expenses associated with the prosecution and maintenance of patent rights following the effective date, and our first right to enforce and defend the patent rights, only apply to the Cas9-II Patent Rights that are subject to our exclusive license, and do not apply to the Cas9-II Patent Rights that are subject only to our non-exclusive license; and

- we have the first right, but not obligation, to enforce the Cas9-II Patent Rights that are subject to our exclusive license, and Broad has the sole and exclusive right, at Broad's expense, to enforce and defend the Cas9-II Patent Rights subject to our non-exclusive license.

Pursuant to the Cas9-II License Agreement, and as of December 31, 2016, we have certain rights under six pending U.S. patent applications, six pending European patent applications, six pending PCT applications, and other related patent applications in jurisdictions outside of the United States and Europe.

### *The General Hospital Corporation License Agreements*

In August 2014, we entered into a license agreement, the First MGH License Agreement, with The General Hospital Corporation, d/b/a Massachusetts General Hospital, or MGH, for specified patent rights, or First License MGH Patent Rights, and specified know-how and biological materials. The First License MGH Patent Rights are directed, in part, to CRISPR/Cas9 and TALE-related compositions of matter and their use for genome editing. Pursuant to the First MGH License Agreement, and as of December 31, 2016, we have certain rights under 12 pending U.S. patent applications, nine pending European patent applications, and other related patent applications in jurisdictions outside of the United States and Europe.

Pursuant to the First MGH License Agreement, MGH granted us an exclusive, worldwide, royalty-bearing, sublicensable license to the First License MGH Patent Rights, to make, have made, use, have used, sell, offer for sale, and import products and processes in the fields of the prevention or treatment of human or animal disease and agriculture, which includes plants and animals bred and raised for human consumption. We refer to these fields as the First MGH Exclusive License Field. Products and processes used for clinical diagnostic assays, and the research, development and sale of research tools, kits, and reagents in the field of agriculture are specifically excluded from our exclusive license to the First License MGH Patent Rights. MGH also granted us a non-exclusive, worldwide, royalty-bearing, sublicensable license to the First License MGH Patent Rights to make, have made, use, have used, sell, offer for sale, and import products and processes in substantially all fields other than the First MGH Exclusive License Field. Products and processes used for clinical diagnostic assays are specifically excluded from our non-exclusive license to the First License MGH Patent Rights. In addition, MGH granted us a non-exclusive, worldwide, royalty-bearing sublicensable license under specified MGH know-how and biological materials to make, have made, use, have used, sell, offer for sale, and import products and processes in all fields, except for products and processes used for clinical diagnostic assays. The licenses granted to us by MGH under the First MGH License Agreement are subject to retained rights of the U.S. government in the First License MGH Patent Rights and a royalty-free right of MGH, academic, and not-for-profit institutions, to practice the First License MGH Patent Rights for educational, research, and clinical purposes.

We are obligated to use commercially reasonable efforts to research, develop, and commercialize products and processes in the exclusive license field and outside the First MGH Exclusive License Field under the First MGH License Agreement. Also, we are required to achieve certain development milestones within specified time periods for products and processes in the First MGH Exclusive License Field and outside the First MGH Exclusive License Field. MGH has the right to terminate our license if we fail to achieve these development milestones.

Under the First MGH License Agreement, we paid MGH an upfront license fee in the low six digit dollar amount and issued less than one percent of our common stock to MGH. We also must pay an annual license maintenance fee ranging from low- to mid-five digit dollar amount, depending on the calendar year, beginning in 2017. We are obligated to reimburse MGH for expenses associated with the prosecution and maintenance of the First License MGH Patent Rights, including expenses associated with any interference proceedings in the USPTO, any opposition proceedings in the EPO, or any other *inter partes* or other post grant proceedings in these or other jurisdictions where we are seeking patent protection.

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MGH is entitled to receive clinical, regulatory, and commercial milestone payments totaling up to \$1.4 million in the aggregate for the first licensed product or process, clinical, and regulatory milestone payments totaling up to \$125,000 in the aggregate for each of the second, third, and fourth indications for which we conduct clinical trials of a licensed product or process and commercial milestone payments totaling up to \$625,000 in the aggregate for each of the second, third, and fourth licensed products or process we introduce into the market. We are obligated to make additional payments to MGH of up to an aggregate of \$1.8 million upon the occurrence of certain sales milestones.

We are also obligated to pay MGH low single-digit percentage royalties on net sales of products for the prevention or treatment of human disease, and ranging from low single-digit to low double-digit percentage royalties on net sales of other products and services made by us, our affiliates, or our sublicensees. The royalty percentage depends on the product and service, and whether such licensed product or licensed service is covered by a valid claim within the First License MGH Patent Rights. If we pay royalties to a third party on net sales of our products, then we can credit up to a mid double-digit percentage of the amount paid to such third party against the royalties due to MGH. Our obligation to pay royalties will expire on a product-by-product and country-by-country basis upon the later of the expiration of the last to expire valid claim of the First License MGH Patent Rights that cover the composition, manufacture or use of each covered product or service in each country or the tenth anniversary of the date of the first commercial sale of the product or service. If we sublicense any of the First License MGH Patent Rights or know-how or materials licensed under the First MGH License Agreement to a third party in the First MGH Exclusive License Field, MGH has the right to receive a low double-digit percentage of the sublicense income, which percentage decreases to a high single-digit percentage after a specified period of time. If we sublicense any of the First License MGH Patent Rights or know-how or materials licensed under the First MGH License Agreement to a third party in the field of research products or processes, MGH has the right to receive a high double-digit percentage of the sublicense income. If we sublicense any of the First License MGH Patent Rights or know-how or materials licensed under the First MGH License Agreement to a third party in any field outside the First MGH Exclusive License Field and outside the field of research products or processes, MGH has the right to receive a low double-digit percentage of the sublicense income.

MGH retains control of the prosecution and maintenance of the First License MGH Patent Rights. We have the right to provide input in the prosecution of the First License MGH Patent Rights, including directing MGH to file and prosecute patents in certain countries. MGH controls the enforcement of the First License MGH Patent Rights, except for the enforcement of the rights exclusively licensed to us, which we control at our expense. We may not enter into any settlement without the prior written consent of MGH. We also retain the first right to defend against any legal or administrative action taken by a third party against a First License MGH Patent Right at our own costs.

Unless terminated earlier, the term of the First MGH License Agreement will expire, on a country-by-country basis, upon the expiration or abandonment of all First License MGH Patent Rights in such country. However, our royalty obligations, discussed above, may survive expiration or termination. We have the right to terminate the First MGH License Agreement at will upon 90 days' written notice to MGH. MGH may terminate the First MGH License Agreement upon a specified period of written notice in the event of our uncured material breach, such notice period varying depending on the nature of the breach. MGH also may terminate the First MGH License Agreement immediately if we challenge the enforceability, validity, or scope of any First License MGH Patent Right or assist a third party to do so, or in the event of our bankruptcy or insolvency.

In August 2016, we entered into a second license agreement, the Second MGH License Agreement, with MGH for specified patent rights, the Second License MGH Patent Rights. Pursuant to the Second MGH License Agreement, and as of December 31, 2016, we have certain rights under one issued U.S. patent, six pending U.S. patent applications, and two pending PCT applications. The Second License MGH Patent Rights are directed, in part, to CRISPR/Cas9 compositions of matter and their use for genome editing.

Pursuant to the Second MGH License Agreement, MGH granted us an exclusive, worldwide, royalty-bearing, sublicensable license to the Second License MGH Patent Rights, to make, have made, use, have used, sell, offer for sale and have sold products and processes in the fields of the prevention and treatment of human and animal disease, or collectively, the Second MGH Exclusive Field. MGH also granted us a non-exclusive, worldwide, royalty-bearing, sublicensable license to use research data and other information pertaining to the Second License MGH Patent Rights to make, have made, use, have used, sell, offer for sale and have sold products and processes in the Second MGH Exclusive

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Field. The licenses granted to us by MGH under the Second MGH License Agreement are subject to retained rights of the U.S. government in the Second License MGH Patent Rights and the royalty-free right of MGH, its affiliates, and academic, government, and not-for-profit institutions to practice the Second License MGH Patent Rights for research and educational purposes.

We are obligated under the Second MGH License Agreement to use commercially reasonable efforts to research, develop, and commercialize products and processes in the Second MGH Exclusive Field. As part of these obligations, we are required to achieve certain development milestones within specified time periods, with MGH having the right to terminate the Second MGH License Agreement if we fail to achieve these milestones within the required time periods.

Under the Second MGH License Agreement, we paid MGH an upfront license fee in the high six digits. We also must pay an annual license maintenance fee beginning in 2018 that increases over time within a specified dollar range in the low six digits, with such maintenance fee being creditable against any royalties due to MGH under the Second MGH License Agreement in the same calendar year. We are obligated to reimburse MGH for expenses associated with the prosecution and maintenance of the Second License MGH Patent Rights.

MGH is entitled to receive clinical and regulatory milestone payments totaling less than \$1 million in the aggregate for up to four licensed products or processes to achieve the specified clinical and regulatory milestones. In addition, MGH is entitled to receive commercial sales milestone payments totaling up to \$4.9 million in the aggregate upon the achievement of milestones relating to first commercial sales of up to four licensed products or processes in the United States and abroad as well as milestones relating to annual net sales of products or processes meeting specified thresholds.

We are also obligated to pay MGH royalties of less than 1% on net sales of products and processes for the prevention or treatment of human disease, and royalties of a low single-digit percentage on net sales of products and processes for the prevention or treatment of a non-human animal disease, made by us, our affiliates, or our sublicensees. Our obligation to pay royalties will expire on a product/process-by-product/process and country-by-country basis upon the later of the expiration of the last to expire valid claim of the Second License MGH Patent Rights that covers the applicable product or process and the tenth anniversary of the date of the first commercial sale of the applicable product or process. The royalty percentages that we are obligated to pay are subject to reduction if at the time of sale the applicable product or process is not covered by a valid claim within the Second License MGH Patent Rights. If we pay royalties to a third party on net sales of a product or process for which a royalty is due under both First MGH License Agreement and the Second MGH License Agreement, we can credit up to a mid double-digit percentage of the amount paid to such third party against the royalties due to MGH under the Second MGH License Agreement, provided that the royalties due to MGH under the Second MGH License Agreement may not be reduced by more than a low to mid double-digit percentage.

Under the Second MGH License Agreement, MGH is also entitled to receive certain payments in the event our market capitalization reaches specified thresholds ranging from low to high ten digit dollar amounts, or MGH Market Cap Success Payments. The MGH Market Cap Success Payments payable to MGH range from a low seven digit dollar amount to a low eight digit dollar amount, which low eight digit dollar amount would be payable only if we achieve at least market capitalization of a high ten digit dollar amount and if we have one licensed product that (i) is the subject of a Phase 1 clinical trial of which we or one of our affiliates or sublicensees is the sponsor, (ii) was the subject of a Phase 1 clinical trial of which we or one of our affiliates or sublicensees was the sponsor with us having determined to conduct a subsequent clinical trial with respect to such product candidate, or (iii) has been approved for sale in either the United States or the European Union. In addition, in the event of an asset sale or merger of our company to a third party for consideration in excess of one or more market capitalization thresholds, we must pay MGH all MGH Market Cap Success Payments corresponding to such market capitalization thresholds that have not previously been paid, or MGH Company Sale Success Payments. MGH Market Cap Success Payments are payable in cash or shares of our common stock at our discretion, and MGH Company Sale Success Payments are payable solely in cash.

MGH retains control of the prosecution and maintenance of the Second License MGH Patent Rights. We have the right to provide input in the prosecution of the Second License MGH Patent Rights, including to direct MGH to file



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and prosecute patents in certain countries at our cost. We control, at our expense, the enforcement of the rights exclusively licensed to us. We may not enter into any settlement without the prior written consent of MGH. We also retain the first right to defend against any legal or administrative action taken by a third party against a Second License MGH Patent Right at our own cost.

Unless terminated earlier, the term of the Second MGH License Agreement will expire upon the expiration or abandonment of all the Second License MGH Patent Rights. However, our royalty obligations may survive expiration or termination. We have the right to terminate the Second MGH License Agreement at will upon 90 days written notice to MGH. MGH may terminate the Second MGH License Agreement upon specified periods of written notice in the event of our uncured material breach, with the length of such notice period varying depending on the nature of the breach. MGH also may terminate the license agreement immediately if we challenge the validity of any Second License MGH Patent Rights or in the event of our bankruptcy or insolvency.

### *Duke University License Agreement*

In October 2014, we entered into a license agreement with Duke University, or Duke, for specified patent right, or Duke Patent Rights, and specified know-how. The Duke Patent Rights are directed, in part, to genome editing approaches, including CRISPR/Cas9 and TALEN approaches, for treating Duchenne muscular dystrophy. Pursuant to this license agreement, and as of December 31, 2016, we have certain rights under three pending U.S. patent applications, two pending European patent applications, and other related patent applications in jurisdictions outside of the United States and Europe.

Pursuant to the license agreement, Duke granted us an exclusive, worldwide, royalty-bearing, sublicensable license to the Duke Patent Rights, to make, have made, use, have used, sell, offer for sale, and import products and services in the field of the prevention or treatment of human disease. Research reagents are specifically excluded from our exclusive license to the Duke Patent Rights. Duke also granted us a non-exclusive and non-sublicensable license to the Duke Patent Rights for internal research in any field, including the research reagent field. In addition, Duke granted us a non-exclusive, worldwide, royalty-bearing sublicensable license under specified Duke know-how to make, have made, use, have used, sell, offer for sale, and import products and processes in field of the prevention or treatment of human disease and specifically excluding the research reagent field. The licenses granted to us by Duke under the license agreement are subject to retained rights of the U.S. government in the Duke Patent Rights and a royalty-free right of Duke to practice or license the Duke Patent Rights for educational, research, and clinical purposes, including the right to provide licenses to governmental laboratories and other non-profit or not-for-profit institutions for non-commercial academic research purposes or other non-commercial, not-for-profit scholarly purposes.

We are obligated to use commercially reasonable efforts to research, develop, and commercialize products and services in the field of the prevention or treatment of human disease. Also, we are required to achieve certain development milestones within specified time periods for products for the treatment of Duchenne muscular dystrophy and for other products in the field of the prevention or treatment of human disease. Duke has the right to terminate our license if we fail to achieve these development milestones.

Pursuant to the license agreement, we paid Duke an upfront license fee in the high five digits. We also must pay an annual license maintenance fee ranging from mid-four digit to low-five digit dollar amount, depending on the calendar year. We are obligated to reimburse Duke for expenses associated with the prosecution and maintenance of the Duke Patent Rights.

Duke is entitled to receive clinical, regulatory, and commercial milestone payments totaling up to \$625,000 in the aggregate per licensed product. We are also obligated to pay to Duke low single-digit percentage royalties based on annual net sales of licensed products and licensed services by us and our affiliates and sublicensees. If we pay royalties to a third party on net sales of a licensed product and the aggregate royalties on the net sales of the licensed product payable to all of our licensors exceeds a specified threshold, then we can credit up to a mid double-digit percentage of the amount paid to such third party against the royalties due to Duke, subject to a limitation on the amounts we may offset against our obligations to Duke that is determined with regard to the pro rata amount of the total royalties payable by us on net sales of the licensed product that are royalties payable to Duke. Our obligation to pay royalties will expire



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on a product-by-product and country-by-country basis upon the later of the expiration of the last to expire valid claim of the Duke Patent Rights that cover the composition, manufacture or use of each covered product or service in each country or the tenth anniversary of the date of the first commercial sale of the product or service. If we sublicense any of the Duke Patent Rights to a third party, Duke has the right to receive a low double-digit percentage of the sublicense income, the percentage of which decreases after we meet certain pre-clinical milestones. To the extent that such sublicense includes a sublicense of rights granted to us from parties other than Duke, we are entitled to assess the relative contributions of the rights licensed under the applicable agreement and apportion to Duke a lower percentage that reflects the portion of the sublicense income attributable to the Duke Patent Rights. In addition, to the extent that our collaboration and license agreement with Juno Therapeutics continues to provide for a sublicense to Juno Therapeutics of the Duke Patent Rights, we have agreed to apportion to Duke no less than a low-single-digit percentage of future non-royalty sublicense income that we receive under the agreement.

Duke controls the prosecution and maintenance of the Duke Patent Rights and will prosecute and maintain the Duke Patent Rights in the United States and in specified foreign countries. We can amend the specified foreign countries to include any jurisdictions we desire to add. If a third party alleges infringement against Duke or us as a result of our or our sublicensee's practice of the Duke Patent Rights or know-how licensed to us under the license agreement, then we will control the litigation and have the obligation to assume all costs. We further have the first right, but not the obligation, to enforce the Duke Patent Rights at our own expense. In the event a third party brings a declaratory judgment action or any other action or defense alleging invalidity of the Duke Patent Rights, then Duke has the right, but not the obligation, to intervene and control the defense of the action at Duke's own expense.

Unless terminated earlier, the term of the license agreement will expire upon on a country-by-country basis, upon the expiration of the last to expire of the Duke Patent Rights in such country. However, our royalty obligations, discussed above, may survive expiration or termination. We have the right to terminate the license agreement at will upon at least two months' written notice to Duke. Duke may terminate the license agreement upon a specified period of written notice in the event of our uncured material breach, such notice period varying depending on the nature of the breach. Duke also may terminate the license agreement upon a specified period of written notice if we challenge the enforceability, validity, or scope of any Duke Patent Right or assist a third party to do so. Duke may terminate the license agreement immediately for our fraud, willful misconduct, or illegal conduct. The license agreement will terminate immediately in the event of our bankruptcy or insolvency.

### **Manufacturing**

We currently contract with third parties for the manufacturing of our materials for preclinical studies and expect to do so for our planned clinical trials. We do not own or operate manufacturing facilities for the production of our program materials. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. The use of contracted manufacturing and reliance on collaboration partners is relatively cost-efficient and has eliminated the need for our direct investment in manufacturing facilities and additional staff early in development. Although we rely on contract manufacturers, we have personnel with manufacturing experience to oversee our contract manufacturers.

To date, our third-party manufacturers have met our manufacturing requirements. We expect third-party manufacturers to be capable of providing sufficient quantities of our program materials to meet anticipated clinical-trial scale demands. To meet our projected needs for commercial manufacturing, third parties with whom we currently work might need to increase their scale of production or we will need to secure alternate suppliers. We believe that there are alternate sources of supply that can satisfy our clinical and commercial requirements, although we cannot be certain that identifying and establishing relationships with such sources, if necessary, would not result in significant delay or material additional costs.

### **Commercialization**

We currently intend to build the commercial infrastructure in the United States and Europe necessary to effectively support the commercialization of all of our programs, if and when we first believe a regulatory approval of a product candidate under one of our programs in a particular geographic market appears probable. The commercial infrastructure for orphan products typically consists of a targeted, specialty sales force that calls on a limited and focused

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group of physicians supported by sales management, medical liaisons, internal sales support, an internal marketing group, and distribution support.

Additional capabilities important to the orphan marketplace include the management of key accounts such as managed care organizations, group purchasing organizations, specialty pharmacies, and government accounts. To develop the appropriate commercial infrastructure, we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that any product candidate we may develop will be approved.

Outside of the United States and Europe, where appropriate, we may elect in the future to utilize strategic partners, distributors, or contract sales forces to assist in the commercialization of our products. In certain instances, we may consider building our own commercial infrastructure.

As product candidates advance through our pipeline, our commercial plans may change. In particular, some of our research programs target potentially larger indications. Data, the size of the development programs, the size of the target market, the size of a commercial infrastructure, and manufacturing needs may all influence our strategies in the United States, Europe, and the rest of the world.

### **Government Regulation**

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, pricing, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products, including biological products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

#### ***Licensure and Regulation of Biologics in the United States***

In the United States, our candidate products would be regulated as biological products, or biologics, under the Public Health Service Act, or PHSA, and the Federal Food, Drug and Cosmetic Act, or FDCA, and its implementing regulations and guidances. The failure to comply with the applicable U.S. requirements at any time during the product development process, including non-clinical testing, clinical testing, the approval process or post-approval process, may subject an applicant to delays in the conduct of the study, regulatory review and approval, and/or administrative or judicial sanctions. These sanctions may include, but are not limited to, the U.S. Food and Drug Administration's, or FDA, refusal to allow an applicant to proceed with clinical testing, refusal to approve pending applications, license suspension, or revocation, withdrawal of an approval, warning letters, adverse publicity, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, and civil or criminal investigations and penalties brought by the FDA or the Department of Justice, or other governmental entities.

An applicant seeking approval to market and distribute a new biologic in the United States generally must satisfactorily complete each of the following steps:

- preclinical laboratory tests, animal studies and formulation studies all performed in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;

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- performance of adequate and well-controlled human clinical trials to establish the safety, potency, and purity of the product candidate for each proposed indication, in accordance with current Good Clinical Practices, or GCP;
- preparation and submission to the FDA of a Biologic License Application, or BLA, for a biologic product requesting marketing for one or more proposed indications, including submission of detailed information on the manufacture and composition of the product in clinical development and proposed labelling;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities, including those of third parties, at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods, and controls are adequate to preserve the product's identity, strength, quality, and purity, and, if applicable, the FDA's current good tissue practice, or GTP, for the use of human cellular and tissue products;
- satisfactory completion of any FDA audits of the non-clinical and clinical trial sites to assure compliance with GCPs and the integrity of clinical data in support of the BLA;
- payment of user fees and securing FDA approval of the BLA and licensure of the new biologic product; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and any post-approval studies required by the FDA.

### *Preclinical Studies and Investigational New Drug Application*

Before testing any biologic product candidate in humans, including a gene therapy product candidate, the product candidate must undergo preclinical testing. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate the potential for efficacy and toxicity in animal studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trials can begin.

As a result, submission of the IND may result in the FDA not allowing the trials to commence or allowing the trial to commence on the terms originally specified by the sponsor in the IND. If the FDA raises concerns or questions either during this initial 30-day period, or at any time during the IND process, it may choose to impose a partial or complete clinical hold. This order issued by the FDA would delay either a proposed clinical study or cause suspension of an ongoing study, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigations may proceed. This could cause significant delays or difficulties in completing planned clinical studies in a timely manner.

With gene therapy protocols, if the FDA allows the IND to proceed, but the Recombinant DNA Advisory Committee, or RAC, of the National Institute of Health, or NIH, 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 also may impose clinical holds on a biologic product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA.

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### *Human Clinical Trials in Support of a BLA*

Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease to be treated under the supervision of a qualified principal investigator in accordance with GCP requirements. Clinical trials are conducted under study protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of the BLA so long as the clinical trial is conducted in compliance with an international guideline for the ethical conduct of clinical research known as the Declaration of Helsinki and/or the laws and regulations of the country or countries in which the clinical trial is performed, whichever provides the greater protection to the participants in the clinical trial.

Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, patient informed consent, ethical factors, the safety of human subjects, and the possible liability of the institution. An IRB must operate in compliance with FDA regulations. The FDA, IRB, or the clinical trial sponsor may suspend or discontinue a clinical trial at any time for various reasons, including a finding that the clinical trial is not being conducted in accordance with FDA requirements or the subjects or patients are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive GCP rules and the requirements for informed consent. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group may recommend continuation of the study as planned, changes in study conduct, or cessation of the study at designated check points based on access to certain data from the study. Finally, research activities involving infectious agents, hazardous chemicals, recombinant DNA, and genetically altered organisms and agents may be subject to review and approval of an Institutional Biosafety Committee in accordance with NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may be required after approval.

- *Phase 1* clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion, and pharmacodynamics in healthy humans or, on occasion, in patients, such as cancer patients.
- *Phase 2* clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials.
- *Phase 3* clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy, and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a biologic; such Phase 3 studies are referred to as “pivotal.”

In some cases, the FDA may approve a BLA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate’s safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional

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experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of biologics approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any Phase 4 clinical trial requirement or to request a change in the product labeling. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

### *Special Regulations and Guidance Governing Gene Therapy Products*

It is possible that the procedures and standards applied to gene therapy products and cell therapy products may be applied to any CRISPR product candidates we may develop, but that remains uncertain at this point. The FDA has defined a gene therapy product as one that mediates its effects by transcription and/or translation of transferred genetic material and/or by integrating into the host genome and which are administered as nucleic acids, viruses, or genetically engineered microorganisms. The products may be used to modify cells *in vivo* or transferred to cells *ex vivo* prior to administration to the recipient. Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. Within the CBER, the review of gene therapy and related products is consolidated in the Office of Cellular, Tissue and Gene Therapies, and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. The CBER works closely with the NIH and the RAC, which makes recommendations to the NIH on gene therapy issues and engages in a public discussion of scientific, safety, ethical, and societal issues related to proposed and ongoing gene therapy protocols. The FDA and the NIH have published guidance documents with respect to the development and submission of gene therapy protocols. The FDA also has published guidance documents related to, among other things, gene therapy products in general, their preclinical assessment, observing subjects involved in gene therapy studies for delayed adverse events, potency testing, and chemistry, manufacturing, and control information in gene therapy INDs.

In addition to the foregoing, products classified as gene therapies are subject to additional regulation. The FDA has issued various guidance documents regarding gene therapies. Although the FDA has indicated that these guidance documents are not legally binding, we believe that our compliance with them is likely necessary to gain approval for any product candidate we may develop. The guidance documents provide additional factors that the FDA will consider at each of the above stages of development and relate to, among other things, the proper preclinical assessment of gene therapies; the chemistry, manufacturing, and control information that should be included in an IND application; the proper design of tests to measure product potency in support of an IND or BLA application; and measures to observe delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high. Further, the FDA usually 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 10 years of annual queries, either in person or by questionnaire.

If a gene therapy trial is conducted at, or sponsored by, institutions receiving the NIH funding for recombinant DNA research, a protocol and related documentation must be submitted to, and the study registered with, the NIH Office of Biotechnology Activities, or OBA, pursuant to the NIH Guidelines for Research Involving Recombinant DNA Molecules prior to the submission of an IND to the FDA. In addition, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. The NIH will convene the Recombinant DNA Advisory Committee, or RAC, a federal advisory committee, to discuss protocols that raise novel or particularly important scientific, safety or ethical considerations at one of its quarterly public meetings. The OBA will notify the FDA of the RAC's decision regarding the necessity for full public review of a gene therapy protocol. RAC proceedings and reports are posted to the OBA web site and may be accessed by the public.

Finally, to facilitate adverse event reporting and dissemination of additional information about gene therapy trials, the FDA and the NIH established the Genetic Modification Clinical Research Information System or GeMCRIS. Investigators and sponsors of a human gene transfer trials can utilize this web-based system to report serious adverse events and annual reports. GeMCRIS also allows members of the public to access basic reports about human gene transfer trials registered with the NIH and to search for information such as trial location, the names of investigators conducting trials, and the names of gene transfer products being studied.

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### *Compliance with cGMP and GTP Requirements*

Before approving a BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in full compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PHSA emphasizes the importance of manufacturing control for products like biologics whose attributes cannot be precisely defined.

For a gene therapy product, the FDA also will not approve the product if the manufacturer is not in compliance with GTP. These standards are found in FDA regulations and guidances that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue based products, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the GTP requirements is to ensure that cell and tissue based products are manufactured in a manner designed to prevent the introduction, transmission, and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through screening and testing.

Manufacturers and others involved in the manufacture and distribution of products must also register their establishments with the FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether foreign or domestic, is deemed misbranded under the FDCA. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. Inspections must follow a “risk-based schedule” that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated.

### *Review and Approval of a BLA*

The results of product candidate development, preclinical testing, and clinical trials, including negative or ambiguous results as well as positive findings, are submitted to the FDA as part of a BLA requesting license to market the product. The BLA must contain extensive manufacturing information and detailed information on the composition of the product and proposed labeling as well as payment of a user fee.

The FDA has 60 days after submission of the application to conduct an initial review to determine whether it is sufficient to accept for filing based on the agency’s threshold determination that it is sufficiently complete to permit substantive review. Once the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has ten months in which to complete its initial review of a standard application and respond to the applicant, and six months for a priority review of the application. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs. The review process may often be significantly extended by FDA requests for additional information or clarification. The review process and the PDUFA goal date may be extended by three months if the FDA requests or if the applicant otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Under the PHSA, the FDA may approve a BLA if it determines that the product is safe, pure, and potent and the facility where the product will be manufactured meets standards designed to ensure that it continues to be safe, pure, and potent.

On the basis of the FDA’s evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA audits of non-clinical and clinical trial sites to assure compliance with GCPs, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. If the application is not approved, the FDA will issue a complete response letter, which will contain the conditions that must be

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met in order to secure final approval of the application, and when possible will outline recommended actions the sponsor might take to obtain approval of the application. Sponsors that receive a complete response letter may submit to the FDA information that represents a complete response to the issues identified by the FDA. Such resubmissions are classified under PDUFA as either Class 1 or Class 2. The classification of a resubmission is based on the information submitted by an applicant in response to an action letter. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has two months to review a Class 1 resubmission and six months to review a Class 2 resubmission. The FDA will not approve an application until issues identified in the complete response letter have been addressed.

The FDA may also refer the application to an advisory committee for review, evaluation, and recommendation as to whether the application should be approved. In particular, the FDA may refer applications for novel biologic products or biologic products that present difficult questions of safety or efficacy to an advisory committee. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates, and provides 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.

If the FDA approves a new product, it may limit the approved indications for use of the product. It may also require that contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may call for post-approval studies, including Phase 4 clinical trials, to further assess the product's safety after approval. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

### *Fast Track, Breakthrough Therapy and Priority Review Designations*

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, and priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the application is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product 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 FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the



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development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

### *Accelerated Approval Pathway*

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

### *Post-Approval Regulation*

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA have imposed as part of the approval process. The sponsor will be required to report certain

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adverse reactions and production problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that 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 lot release, the manufacturer must submit samples of each lot, 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, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency, and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the 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 a product, including adverse events of unanticipated severity or frequency, or with 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 trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- 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. Pharmaceutical 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.

### *Orphan Drug Designation*

Orphan drug designation in the United States is designed to encourage sponsors to develop products intended for rare diseases or conditions. In the United States, a rare disease or condition is statutorily defined as a condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available the biologic for the disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation qualifies a company for tax credits and market exclusivity for seven years following the date of the product's marketing approval if granted by the FDA. An application for designation as an orphan product

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can be made any time prior to the filing of an application for approval to market the product. A product becomes an orphan when it receives orphan drug designation from the Office of Orphan Products Development, or OOPD, at the FDA based on acceptable confidential requests made under the regulatory provisions. The product must then go through the review and approval process like any other product.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first drug. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation.

The period of exclusivity begins on the date that the marketing application is approved by the FDA and applies only to the indication for which the product has been designated. The FDA may approve a second application for the same product for a different use or a second application for a clinically superior version of the product for the same use. The FDA cannot, however, approve the same product made by another manufacturer for the same indication during the market exclusivity period unless it has the consent of the sponsor or the sponsor is unable to provide sufficient quantities.

### *Pediatric Studies and Exclusivity*

Under the Pediatric Research Equity Act of 2003, a BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product 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. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

### *Biosimilars and Exclusivity*

The 2010 Patient Protection and Affordable Care Act, which was signed into law in March 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. To date, four biosimilar products have been approved by the FDA for use in the United States. No interchangeable biosimilars, however, have been approved. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Additional guidances are expected to be finalized by the FDA in the near term.

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Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is “biosimilar to” or “interchangeable with” a previously approved biological product or “reference product.” In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such 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.

### *Patent Term Restoration and Extension*

A patent claiming a new biologic product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of a clinical investigation involving human beings is begun and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product’s approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

### *FDA Approval of Companion Diagnostics*

In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, for novel drugs, a companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product’s labeling. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. Under the FDCA, *in vitro* diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution.

### *Regulation and Procedures Governing Approval of Medicinal Products in the European Union*

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the European Union generally

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follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by these authorities before the product can be marketed and sold in the European Union.

### *Clinical Trial Approval*

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on GCP, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member states. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application, or CTA, must be accompanied by an investigational medicinal product dossier with supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and corresponding national laws of the member states and further detailed in applicable guidance documents.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation (EU) No 536/2014 will become applicable no earlier than May 28, 2016. It will overhaul the current system of approvals for clinical trials in the European Union. Specifically, the new legislation, which will be directly applicable in all member states, aims at simplifying and streamlining the approval of clinical trials in the European Union. For instance, the New Clinical Trials Regulation provides for a streamlined application procedure via a single entry point and strictly defined deadlines for the assessment of clinical trial applications.

### *Marketing Authorization*

To obtain a marketing authorization for a product under the European Union regulatory system, an applicant must submit an MAA, either under a centralized procedure administered by the European Medicines Authority, or EMA, or one of the procedures administered by competent authorities in European Union Member States (decentralized procedure, national procedure, or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the European Union. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the European Union, an applicant must demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Specifically, the grant of marketing authorization in the European Union for products containing viable human tissues or cells such as gene therapy medicinal products is governed by Regulation 1394/2007/EC on advanced therapy medicinal products, read in combination with Directive 2001/83/EC of the European Parliament and of the Council, commonly known as the Community code on medicinal products. Regulation 1394/2007/EC lays down specific rules concerning the authorization, supervision, and pharmacovigilance of gene therapy medicinal products, somatic cell therapy medicinal products, and tissue engineered products. Manufacturers of advanced therapy medicinal products must demonstrate the quality, safety, and efficacy of their products to EMA which provides an opinion regarding the application for marketing authorization. The European Commission grants or refuses marketing authorization in light of the opinion delivered by EMA.

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Under the centralized procedure, the Committee for Medicinal Products for Human Use, or CHMP, established at the EMA is responsible for conducting an initial assessment of a product. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts such a request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that it is no longer appropriate to conduct an accelerated assessment.

### *Regulatory Data Protection in the European Union*

In the European Union, new chemical entities approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Regulation (EC) No 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for a period of eight years. During the additional two-year period of market exclusivity, a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will 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 authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

### *Periods of Authorization and Renewals*

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To that end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the drug on the EU market (in the case of the centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid.

### *Regulatory Requirements after Marketing Authorization*

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product. These include compliance with the European Union's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. In addition, the manufacturing of authorized products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's GMP requirements and comparable requirements of other regulatory bodies in the European Union, which mandate the methods, facilities, and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. Finally, the marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union under Directive 2001/83EC, as amended.

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### *Orphan Drug Designation and Exclusivity*

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the drug will be of significant benefit to those affected by that condition.

An orphan drug designation provides a number of benefits, including fee reductions, regulatory assistance, and the possibility to apply for a centralized European Union marketing authorization. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, neither the EMA nor the European Commission or the member states can accept an application or grant a marketing authorization for a “similar medicinal product.” A “similar medicinal product” is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may, however, 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 drug designation because, for example, the product is sufficiently profitable not to justify market exclusivity.

### ***Coverage, Pricing, and Reimbursement***

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may seek regulatory approval by the FDA or other government authorities. 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 any product candidates we may develop unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of such product candidates. Even if any product candidates we may develop are approved, sales of such product candidates will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers, and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such product candidates. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. 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 approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover any product candidates we may develop could reduce physician utilization of such product candidates once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payor’s decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor’s determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of pharmaceuticals have been a focus in this effort. Governments have shown significant interest in



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implementing cost-containment programs, including price controls, restrictions on reimbursement, and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for any product candidates we may develop will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of any product candidates we may develop to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies (so called health technology assessments, or HTAs) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic, and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade (arbitrage between low-priced and high-priced member states), can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

### ***Healthcare Law and Regulation***

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of pharmaceutical products that are granted marketing approval. Arrangements with providers, consultants, third-party payors, and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving, or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious, or

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fraudulent or knowingly making, using, or causing to made or used a false record or statement to avoid, decrease, or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, or PPACA, as amended by the Health Care Education Reconciliation Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring pharmaceutical manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

### ***Healthcare Reform***

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the PPACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the PPACA of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;

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- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price", or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable products to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient products to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products. However, the IPAB implementation has been not been clearly defined. The PPACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription product spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted in the United States since the PPACA was enacted. For example, 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 2012 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 up to 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, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers, and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

With the new Administration and Congress, there will likely be additional legislative changes, including repeal and replacement of certain provisions of the PPACA. It remains to be seen, however, precisely what the new legislation will provide, when it will be enacted and what impact it will have on the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop product candidates.

There have been, and likely will continue to be, additional 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. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop product candidates.

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***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 Conservation and Recovery Act, and the Toxic Substances Control Act, affect our business. These and other laws govern the use, handling, and disposal of various biologic, chemical, and radioactive substances used in, and wastes generated by, 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. Equivalent laws have been adopted in third countries that impose similar obligations.

**Employees**

As of January 1, 2017, we had 89 full-time employees, including 37 employees with M.D. or Ph.D. degrees. Of these full-time employees, 63 employees are engaged in research and development activities. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

**Our Corporate Information**

We were incorporated under the name Gengine, Inc. in Delaware in September 2013, and we changed our name to Editas Medicine, Inc. in November 2013. Our executive offices are located at 11 Hurley St., Cambridge, Massachusetts, 02141, and our telephone number is (617) 401-9000.

**Available Information**

We maintain an internet website at [www.editasmedicine.com](http://www.editasmedicine.com) and make available free of charge through our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act of 1934, or the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the Securities and Exchange Commission, or the SEC. You can find, copy and inspect information we file at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's public reference room. You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at <http://www.sec.gov>. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investors & Media," as a source of information about us.

The information on our website is not incorporated by reference into this Annual Report on Form 10-K and should not be considered to be a part of this Annual Report on Form 10-K. Our website address is included in this Annual Report on Form 10-K as an inactive technical reference only.

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**Item 1A. Risk Factors**

Our business is subject to numerous risks. The following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in this Annual Report on Form 10-K and other filings with the Securities and Exchange Commission, or the SEC, press releases, communications with investors, and oral statements. Actual future results may differ materially from those anticipated in our forward-looking statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events, or otherwise.

**Risks Related to Our Financial Position and Need for Additional Capital**

*We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.*

Since inception, we have incurred significant operating losses. Our net losses were \$97.2 million, \$72.9 million and \$13.7 million, for the years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016, we had an accumulated deficit of \$185.5 million. We have financed our operations primarily through the public offering of our common stock, private placements of our preferred stock, an equipment loan, our collaboration with Juno Therapeutics, Inc., or Juno Therapeutics, and our agreement with Cystic Fibrosis Foundation Therapeutics, Inc., or CFFT. We have devoted all of our efforts to research and development. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- continue our current research programs and our preclinical development of product candidates from our current research programs;
- seek to identify additional research programs and additional product candidates;
- initiate preclinical testing and clinical trials for any product candidates we identify and develop;
- maintain, expand, and protect our intellectual property portfolio and provide reimbursement of third-party expenses related to our patent portfolio;
- seek marketing approvals for any of our product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing, and distribution infrastructure to commercialize any medicines for which we may obtain marketing approval;
- further develop our genome editing platform;
- hire additional clinical, quality control, and scientific personnel;
- add operational, financial, and management information systems and personnel, including personnel to support our product development;
- acquire or in-license other medicines and technologies;
- validate a commercial-scale current Good Manufacturing Practices, or cGMP, manufacturing facility; and
- operate as a public company.

We have not initiated clinical development of any product candidate and expect that it will be many years, if ever, before we have a product candidate ready for commercialization. To become and remain profitable, we must

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develop and eventually commercialize a medicine or medicines with significant market potential. This will require us to be successful in a range of challenging activities, including identifying product candidates, completing preclinical testing and clinical trials of product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing, and selling those medicines for which we may obtain marketing approval, and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. We are currently only in the preclinical testing stages for our most advanced research programs. 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 could cause our stockholders to lose all or part of their investments in us.

***We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce, or eliminate our research and product development programs or commercialization efforts.***

We expect our expenses to increase in connection with our ongoing activities, particularly as we identify, continue the research and development of, initiate clinical trials of, and seek marketing approval for, product candidates. In addition, if we obtain marketing approval for any product candidates we may develop, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution to the extent that such sales, marketing, manufacturing, and distribution are not the responsibility of a collaborator. In 2016 we incurred, and in future years we expect to continue to incur, significant costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, or eliminate our research and product development programs or future commercialization efforts.

We expect that our existing cash and cash equivalents at December 31, 2016, anticipated interest income, anticipated research support under our collaboration agreement with Juno Therapeutics, anticipated payments from CFFT, and anticipated payments from our subtenant will enable us to fund our operating expenses and capital expenditure requirements for at least the next 18 months following the date of this Annual Report on Form 10-K. Our future capital requirements will depend on many factors, including:

- the scope, progress, results, and costs of drug discovery, preclinical development, laboratory testing, and clinical trials for the product candidates we may develop;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights, and defending intellectual property-related claims;
- the costs, timing, and outcome of regulatory review of the product candidates we may develop;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing, and distribution, for any product candidates for which we receive regulatory approval;
- the success of our collaboration with Juno Therapeutics;
- whether Juno Therapeutics exercises either or both of its options to extend the research program term under our collaboration (each of which would trigger an extension payment to us);
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the extent to which we acquire or in-license other medicines and technologies;
- the costs of reimbursing our licensors for the prosecution and maintenance of the patent rights in-licensed by us; and

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- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive, and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, even if we successfully identify and develop product candidates and those are approved, we may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of medicines that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

***Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.***

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, and licensing arrangements. We do not have any committed external source of funds, other than our collaboration with Juno Therapeutics, our agreement with CFFT, and our sublease, each of which is limited in scope and duration. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our stockholders may be materially diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt 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 raise funds through additional collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates, or we may have to 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.

***Our short operating history may make it difficult for our stockholders to evaluate the success of our business to date and to assess our future viability.***

We are an early-stage company. We were founded and commenced operations in the second half of 2013. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our technology, identifying potential product candidates, and undertaking preclinical studies. All of our research programs are still in the preclinical or research stage of development, and their risk of failure is high. We have not yet demonstrated an ability to initiate or successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale medicine, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes about 10 to 15 years to develop a new medicine from the time it is discovered to when it is available for treating patients. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays, and other known and unknown factors. We will need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect that our financial condition and operating results will continue to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, our stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.



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***We have never generated revenue from product sales and may never be profitable.***

Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaborative partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, product candidates we may identify for development. We do not anticipate generating revenues from product sales for the next several years, if ever. Our ability to generate future revenues from product sales depends heavily on our, or our collaborators', ability to successfully:

- identify product candidates and complete research and preclinical and clinical development of any product candidates we may identify;
- seek and obtain regulatory and marketing approvals for any of our product candidates for which we complete clinical trials;
- launch and commercialize any of our product candidates for which we obtain regulatory and marketing approval by establishing a sales force, marketing, and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- qualify for adequate coverage and reimbursement by government and third-party payors for any our product candidates for which we obtain regulatory and marketing approval;
- develop, maintain, and enhance a sustainable, scalable, reproducible, and transferable manufacturing process for the product candidates we may develop;
- establish and maintain supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and the market demand for any of our product candidates for which we obtain regulatory and marketing approval;
- obtain market acceptance of any product candidates we may develop as viable treatment options;
- address competing technological and market developments;
- implement internal systems and infrastructure, as needed;
- negotiate favorable terms in any collaboration, licensing, or other arrangements into which we may enter and performing our obligations in such collaborations;
- maintain, protect, and expand our portfolio of intellectual property rights, including patents, trade secrets, and know-how;
- avoid and defend against third-party interference or infringement claims; and
- attract, hire, and retain qualified personnel.

Even if one or more of the product candidates we may develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or other regulatory authorities to perform clinical and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

## Risks Related to Discovery, Development, and Commercialization

***We intend to identify and develop product candidates based on a novel genome editing technology, which makes it difficult to predict the time and cost of product candidate development. No products that utilize genome editing technology have been approved in the United States or in Europe, and there have only been a limited number of human clinical trials of a genome editing product candidate.***

We have concentrated our research and development efforts on our genome editing platform, which uses CRISPR technology. Our future success depends on the successful development of this novel genome editing therapeutic approach. To date, no product that utilizes genome editing, including CRISPR technology, has been approved in the United States or Europe and there have been only a limited number of clinical trials involving the use of a therapeutic utilizing genome editing technologies. For example, we are aware of a limited number of groups initiating clinical trials using CRISPR technology. Because our programs are all in the research or preclinical stage, we have not yet been able to assess safety in humans, and there may be long-term effects from treatment with any of our future product candidates that we cannot predict at this time. Any product candidates we may develop will act at the level of DNA, and, because animal DNA differs from human DNA, it will be difficult for us to test our future product candidates in animal models for either safety or efficacy. Also, animal models do not exist for some of the diseases we expect to pursue in our programs. As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our genome editing platform, or any similar or competitive genome editing platforms, will result in the identification, development, and regulatory approval of any medicines. There can be no assurance that any development problems we experience in the future related to our genome editing platform or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays in developing a sustainable, reproducible, and scalable manufacturing process or transferring that process to commercial partners. Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

***Because genome editing is novel and the regulatory landscape that will govern any product candidates we may develop is uncertain and may change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop.***

The regulatory requirements that will govern any novel genome editing product candidates we develop are not entirely clear and may change. Within the broader genomic medicine field, we are aware of at least two gene therapy products that have received marketing authorization from the European Commission, and no gene therapy products have received marketing approval in the United States. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. Regulatory requirements governing gene therapy products and cell therapy products have changed frequently and will likely continue to change in the future. Moreover, there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the United States, the FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at the institution participating in the clinical trial. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the United States National Institutes of Health, or NIH, are also subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation. The same applies in the European Union. The EMA's Committee for Advanced Therapies, or CAT, is responsible for assessing the quality, safety, and efficacy of advanced-therapy medicinal products. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the EMA. In the European Union, the development and evaluation of a gene therapy medicinal product must be considered in the context of the relevant European Union guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal

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products and require that we comply with these new guidelines. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any CRISPR product candidates we may develop, but that remains uncertain at this point.

Adverse developments in clinical trials conducted by others of gene therapy products, cell therapy products, or products developed through the application of a CRISPR or other genome editing technology may cause the FDA, the EMA, and other regulatory bodies to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing genome editing technologies, either of which could materially harm our business. In addition, the clinical trial requirements of the FDA, the EMA, and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known, or more extensively studied pharmaceutical or other product candidates. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing genome editing technology in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays, or other impediments to our research programs or the commercialization of resulting products.

The regulatory review committees and advisory groups described above and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates, or lead to significant post-approval limitations or restrictions. As we advance our research programs and develop future product candidates, we will be required to consult with these regulatory and advisory groups and to comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of any product candidates we identify and develop.

### ***Adverse public perception of genomic medicines, and genome editing in particular, may negatively impact regulatory approval of, or demand for, our potential products.***

Our potential therapeutic products involve editing the human genome. The clinical and commercial success of our potential products will depend in part on public acceptance of the use of genome editing therapy for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that genome editing is unsafe, unethical, or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

In addition, genome editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns relating to the application of genome editing technology to human embryos or the human germline. For example, in April 2015, Chinese scientists reported on their attempts to edit the genome of human embryos to modify the gene for hemoglobin beta. This is the gene in which a mutation occurs in patients with the inherited blood disorder beta thalassemia. Although this research was purposefully conducted in embryos that were not viable, the work prompted calls for a moratorium or other types of restrictions on genome editing of human eggs, sperm, and embryos. The Alliance for Regenerative Medicine in Washington has called for a voluntary moratorium on the use of genome editing technologies, including CRISPR/Cas9, in research that involved altering human embryos or human germline cells. Similarly, the NIH has announced that it would not fund any use of genome editing technologies in human embryos, noting that there are multiple existing legislative and regulatory prohibitions against such work, including the Dickey-Wicker Amendment, which prohibits the use of appropriated funds for the creation of human embryos for research purposes or for research in which human embryos are destroyed. While the National Academy of Sciences released a report in February 2017 suggesting that it may be advisable to permit clinical trials for germline genome editing if undertaken for compelling reasons and under strict oversight, it maintained that any such research should only proceed with broad public input. Laws in the United Kingdom prohibit genetically modified embryos from being implanted into women, but embryos can be altered in research labs under license from the Human Fertilisation and Embryology Authority. Research on embryos is more tightly controlled in many other European countries.

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Moreover, in an annual worldwide threat assessment report delivered to the U.S. Congress in February 2016, the U.S. Director of National Intelligence stated that research into genome editing probably increases the risk of the creation of potentially harmful biological agents or products, including weapons of mass destruction. He noted that the broad distribution, low cost, and accelerated pace of development of genome editing technology could result in the deliberate or unintentional misuse of such technology.

Although we do not use our technologies to edit human embryos or the human germline, such public debate about the use of genome editing technologies in human embryos and heightened regulatory scrutiny could prevent or delay our development of product candidates. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair our development and commercialization of product candidates or demand for any products we may develop. Adverse events in our preclinical studies or clinical trials or those of our competitors or of academic researchers utilizing genome editing technologies, even if not ultimately attributable to product candidates we may identify and develop, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of potential product candidates we may identify and develop, stricter labeling requirements for those product candidates that are approved, and a decrease in demand for any such product candidates. Use of genome editing technology by a third party or government to develop biological agents or products that threaten the United States' national security could similarly result in such negative impacts to us.

### ***We may not be successful in our efforts to identify, develop, or commercialize potential product candidates.***

The success of our business depends primarily upon our ability to identify, develop, and commercialize products based on our genome editing platform. All of our product development programs are still in the preclinical or research stage of development. Our research programs, including those subject to our collaboration with Juno Therapeutics and our agreement with CFFT, may fail to identify potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates, or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products impractical to manufacture, unmarketable, or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business, financial condition, results of operations, and prospects. Research programs to identify new product candidates require substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

### ***The genome editing field is relatively new and is evolving rapidly. We are focusing our research and development efforts on CRISPR gene editing technology using Cas9 and Cpf1 enzymes, but other genome editing technologies may be discovered that provide significant advantages over CRISPR/Cas9 or CRISPR/Cpf1, which could materially harm our business.***

To date, we have focused our efforts on genome editing technologies using CRISPR and the Cas9 and Cpf1 enzymes. Other companies have previously undertaken research and development of genome editing technologies using zinc finger nucleases, engineered meganucleases, and transcription activator-like effector nucleases, or TALENs, but to date none has obtained marketing approval for a product candidate. There can be no certainty that the CRISPR/Cas9 or CRISPR/Cpf1 technology will lead to the development of genomic medicines, that other genome editing technologies will not be considered better or more attractive for the development of medicines or that either Cas9 or Cpf1, the two CRISPR associated proteins that we use, may be useful or successful in developing therapeutics. For example, Cas9 or Cpf1 may be determined to be less attractive than other CRISPR enzymes, including CRISPR enzymes that have yet to be discovered. Similarly, a new genome editing technology that has not been discovered yet may be determined to be more attractive than CRISPR. Moreover, if we decide to develop genome technologies other than CRISPR technology using a Cas9 or Cpf1 enzyme, we cannot be certain we will be able to obtain rights to such technologies. Although all of our founders who currently provide consulting and advisory services to us in the areas of Cas9 and TALEN genome editing technologies have assignment of inventions obligations to us with respect to the services they perform for us, these assignment of inventions obligations are subject to limitations and do not extend to their work in other fields or to

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the intellectual property arising from their employment with their respective academic and research institutions. To obtain intellectual property rights assigned by these founders to such institutions, we would need to enter into license agreements with such institutions. Any of these factors could reduce or eliminate our commercial opportunity, and could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***We depend heavily on the success of our most advanced program. All of our product development programs are at the preclinical or research stage. Preclinical testing and clinical trials of product candidates may not be successful. If we are unable to commercialize any product candidates we may develop or experience significant delays in doing so, our business will be materially harmed.***

We have invested a significant portion of our efforts and financial resources in the identification of our most advanced product development program for the treatment of Leber Congenital Amaurosis, or LCA, type 10, or LCA10. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of a product candidate for the treatment of LCA10 and other product candidates that we may identify in the future. The success of product candidates we may identify and develop will depend on many factors, including the following:

- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials for our most advanced program;
- successful completion of preclinical studies and investigational new drug, or IND, -enabling studies;
- successful enrollment in, and completion of, clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity for our medicines;
- launching commercial sales of the medicines, if and when approved, whether alone or in collaboration with others;
- acceptance of the medicines, if and when approved, by patients, the medical community, and third-party payors;
- effectively competing with other therapies and treatment options;
- a continued acceptable safety profile of the medicines following approval;
- enforcing and defending intellectual property and proprietary rights and claims; and
- achieving desirable medicinal properties for the intended indications.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize any product candidates we may develop, which would materially harm our business.

Of the large number of biologics and drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a Biologics License Application, or BLA, to the FDA or a marketing authorization application, or MAA, to the EMA. Not all BLAs or MAAs that are submitted to a regulatory agency are approved for commercialization. Furthermore, even if we do receive regulatory approval to market any product candidates that we

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may identify and develop, any such approval may be subject to limitations on the indicated uses for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our research programs, we cannot assure you that we will successfully develop or commercialize our most advanced program, or any of our other research programs. If we or any of our future development partners are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize, any product candidates we may identify and develop, we may not be able to generate sufficient revenue to continue our business.

***If serious adverse events, undesirable side effects, or unexpected characteristics are identified during the development of any product candidates we may develop, we may need to abandon or limit our further clinical development of those product candidates.***

We have not evaluated any product candidates in human clinical trials, and our proposed delivery modes have never been evaluated in combination with CRISPR technology in human clinical trials. It is impossible to predict when or if any product candidates we may develop will prove safe in humans. In the genomic medicine field, there have been several significant adverse events from gene therapy treatments in the past, including reported cases of leukemia and death. There can be no assurance that genome editing technologies will not cause undesirable side effects.

A significant risk in any genome editing product is that the edit will be “off-target” and cause serious adverse events, undesirable side effects, or unexpected characteristics. For example, off-target cuts could lead to disruption of a gene or a genetic regulatory sequence at an unintended site in the DNA, or, in those instances where we also provide a segment of DNA to serve as a repair template, it is possible that following off-target cut events, DNA from such repair template could be integrated into the genome at an unintended site, potentially disrupting another important gene or genomic element. We cannot be certain that off-target editing will not occur in any of our planned or future clinical studies. There is also the potential risk of delayed adverse events following exposure to genome editing therapy due to the potential for persistent biological activity of the genetic material or other components of products used to carry the genetic material.

If any product candidates we develop are associated with serious adverse events, or undesirable side effects, or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk-benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations, and prospects. Many product candidates that initially showed promise in early stage testing for treating cancer or other diseases have later been found to cause side effects that prevented further clinical development of the product candidates.

***If any of the product candidates we may develop or the delivery modes we rely on cause undesirable side effects, it could delay or prevent their regulatory approval, limit the commercial potential, or result in significant negative consequences following any potential marketing approval.***

Product candidates we may develop may be associated with off-target editing or other serious adverse events, undesirable side effects, or unexpected characteristics. There also is the potential risk of delayed adverse events following exposure to gene editing therapy due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material. In addition to serious adverse events or side effects caused by any product candidate we may develop, the administration process or related procedures also can cause undesirable side effects. If any such events occur, our clinical trials could be suspended or terminated.

If in the future we are unable to demonstrate that such adverse events were caused by factors other than our product candidate, the FDA, the European Commission, the EMA or other regulatory authorities could order us to cease further development of, or deny approval of, any product candidates we are able to develop for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any product candidate we may develop, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to identify and

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develop product candidates, and may harm our business, financial condition, result of operations, and prospects significantly.

Additionally, if we successfully develop a product candidate and it receives marketing approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy, or REMS, to ensure that the benefits of treatment with such product candidate outweighs the risks for each potential patient, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients, a communication plan to health care practitioners, extensive patient monitoring, or distribution systems and processes that are highly controlled, restrictive, and more costly than what is typical for the industry. Furthermore, if we or others later identify undesirable side effects caused by any product candidate that we to develop, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of any product candidates we may identify and develop and could have a material adverse effect on our business, financial condition, results of operations, and prospects.

### ***We have not tested any of our proposed delivery modes and product candidates in clinical trials.***

Our proposed delivery modes, combined with our product candidates, have never been evaluated in human clinical trials, although we are aware of one group in China that has begun a clinical trial where cells modified by CRISPR/Cas9 have been administered to a patient in China and one group in the United States that is seeking to initiate clinical studies using CRISPR/Cas9 in the United States. Any product candidates we develop may fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical trials.

There is a high failure rate for drugs and biologics proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit, or prevent regulatory approval. In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development.

Any such adverse events may cause us to delay, limit, or terminate planned clinical trials, any of which would have a material adverse effect on our business, financial condition, results of operations, and prospects.

### ***Because we are developing product candidates for the treatment of diseases in which there is little clinical experience using new technologies, there is increased risk that the FDA, the EMA, or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results and that these results may be difficult to analyze.***

During the regulatory review process, we will need to identify success criteria and endpoints such that the FDA, the EMA, or other regulatory authorities will be able to determine the clinical efficacy and safety profile of any product



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candidates we may develop. As we are initially seeking to identify and develop product candidates to treat diseases in which there is little clinical experience using new technologies, there is heightened risk that the FDA, the EMA, or other regulatory authorities may not consider the clinical trial endpoints that we propose to provide clinically meaningful results (reflecting a tangible benefit to patients). In addition, the resulting clinical data and results may be difficult to analyze. Even if the FDA does find our success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoints to a degree of statistical significance. This may be a particularly significant risk for many of the genetically defined diseases for which we plan to develop product candidates because many of these diseases have small patient populations, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. Further, even if we do achieve the pre-specified criteria, we may produce results that are unpredictable or inconsistent with the results of the non-primary endpoints or other relevant data. The FDA also weighs the benefits of a product against its risks, and the FDA may view the efficacy results in the context of safety as not being supportive of regulatory approval. Other regulatory authorities in the European Union and other countries, such as the CAT, may make similar comments with respect to these endpoints and data. Any product candidates we may develop will be based on a novel technology that makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval. No genome editing product has been approved in the United States or in Europe.

***If clinical trials of any product candidates we may identify and develop fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.***

Before obtaining marketing approval from regulatory authorities for the sale of any product candidates we may identify and develop, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy in humans of any such product candidates. Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. A failure of one or more clinical trials can occur 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. 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 product candidates.

We or our collaborators may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize any product candidates we may identify and develop, including:

- delays in reaching a consensus with regulators on trial design;
- regulators, institutional review boards, or IRBs, or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- delays in reaching or failing to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective contract research organizations, or CROs, and clinical trial sites;
- clinical trials of any product candidates we may develop may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development or research programs;
- difficulty in designing well-controlled clinical trials due to ethical considerations which may render it inappropriate to conduct a trial with a control arm that can be effectively compared to a treatment arm;

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- difficulty in designing clinical trials and selecting endpoints for diseases that have not been well-studied and for which the natural history and course of the disease is poorly understood;
- the number of patients required for clinical trials of any product candidates we may develop may be larger than we anticipate; enrollment of suitable participants in these clinical trials, which may be particularly challenging for some of the rare genetically defined diseases we are targeting in our most advanced programs, may be delayed or slower than we anticipate; or subjects may drop out of these clinical trials 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;
- regulators, IRBs, or independent ethics committees may require that we or our investigators suspend or terminate clinical research or clinical trials of any product candidates we may develop for various reasons, including noncompliance with regulatory requirements, a finding of undesirable side effects or other unexpected characteristics, or that the participants are being exposed to unacceptable health risks or after an inspection of our clinical trial operations or trial sites;
- the cost of clinical trials of any product candidates we may develop may be greater than we anticipate;
- the supply or quality of any product candidates we may develop or other materials necessary to conduct clinical trials of any product candidates we may develop may be insufficient or inadequate, including as a result of delays in the testing, validation, manufacturing, and delivery of any product candidates we may develop to the clinical sites by us or by third parties with whom we have contracted to perform certain of those functions;
- delays in having subjects complete participation in a trial or return for post-treatment follow-up;
- clinical trial sites dropping out of a trial;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- occurrence of serious adverse events associated with any product candidates we may develop that are viewed to outweigh their potential benefits;
- occurrence of serious adverse events in trials of the same class of agents conducted by other sponsors; and
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

If we or our collaborators are required to conduct additional clinical trials or other testing of any product candidates we may develop beyond those that we currently contemplate, if we or our collaborators are unable to successfully complete clinical trials of any product candidates we may develop or other testing, or if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we or our collaborators may:

- be delayed in obtaining marketing approval for any such product candidates we may develop or not obtain marketing approval 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, including boxed warnings;

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- be subject to changes in the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy;
- be sued; or
- experience damage to our reputation.

Product development costs will also increase if we or our collaborators experience delays in testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize any product candidates we may develop, could allow our competitors to bring products to market before we do, and could impair our ability to successfully commercialize any product candidates we may develop, any of which may harm our business, financial condition, results of operations, and prospects.

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

We or our collaborators may not be able to initiate or continue clinical trials for any product candidates we identify or develop 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 analogous regulatory authorities outside the United States, or as needed to provide appropriate statistical power for a given trial. Enrollment may be particularly challenging for some of the rare genetically defined diseases we are targeting in our most advanced programs. In addition, if patients are unwilling to participate in our gene editing trials because of negative publicity from adverse events related to the biotechnology, gene therapy, or genome editing fields, competitive clinical trials for similar patient populations, clinical trials in competing products, or for other reasons, the timeline for recruiting patients, conducting studies, and obtaining regulatory approval of any product candidates we may develop may be delayed. Moreover, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as any product candidates we may develop, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- size of the patient population and process for identifying subjects;
- design of the trial protocol;
- availability and efficacy of approved medications for the disease under investigation;
- availability of genetic testing for potential patients;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- eligibility and exclusion criteria for the trial in question;

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- perceived risks and benefits of the product candidate under trial;
- perceived risks and benefits of genome editing as a therapeutic approach;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

In particular, our most advanced programs are focused on rare genetically defined diseases with limited patient pools from which to draw for enrollment in clinical trials. For example, the global incidence of LCA10 is estimated to be two to three per 100,000 live births worldwide. The eligibility criteria of our clinical trials will further limit the pool of available trial participants. Additionally, the process of finding and diagnosing patients may prove costly.

Our ability to successfully initiate, enroll, and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- different standards for the conduct of clinical trials;
- different standard-of-care for patients with a particular disease;
- inability to locate qualified local consultants, physicians, and partners; and
- potential burden of complying with a variety of foreign laws, medical standards, and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

Enrollment delays in our clinical trials may result in increased development costs for any product candidates we may develop, which would cause the value of our company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit, or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business, financial condition, results of operations, and prospects.

***We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications among many potential options. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial medicines or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable medicines. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing, or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Any such event could have a material adverse effect on our business, financial condition, results of operations, and prospects.

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***If we are unable to successfully identify patients who are likely to benefit from therapy with any medicines we develop, or experience significant delays in doing so, we may not realize the full commercial potential of any medicines we may develop.***

Our success may depend, in part, on our ability to identify patients who are likely to benefit from therapy with any medicines we may develop, which requires those potential patients to have their DNA analyzed for the presence or absence of a particular sequence. For example, although LCA can be diagnosed based on a patient's symptoms and retinal scans, DNA samples are taken from LCA patients in order to test for the presence of the known gene mutations that cause LCA and, where possible, to identify the specific genetically defined disease, such as LCA10. If we, or any third parties that we engage to assist us, are unable to successfully identify such patients, or experience delays in doing so, then:

- our ability to develop any product candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;
- any product candidates we develop may not receive marketing approval if safe and effective use of such product candidates depends on an *in vitro* diagnostic; and
- we may not realize the full commercial potential of any product candidates we develop that receive marketing approval if, among other reasons, we are unable to appropriately select patients who are likely to benefit from therapy with our medicines.

As a result, we may be unable to successfully develop and realize the commercial potential of any product candidates we may identify and develop, and our business, financial condition, results of operations, and prospects would be materially adversely effected.

***Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize a product candidate we may develop, and any such approval may be for a more narrow indication than we seek.***

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if any product candidates we may develop meet their safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials, and the review process.

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Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings or a REMS. These regulatory authorities may require precautions or contra-indications with respect to conditions of use, or they may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of any product candidates we may develop. Any of the foregoing scenarios could materially harm the commercial prospects for any product candidates we may develop and materially adversely affect our business, financial condition, results of operations, and prospects.

***Even if any product candidates we may develop receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors, and others in the medical community necessary for commercial success.***

The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors, and others in the medical community. Ethical, social, and legal concerns about genomic medicines generally and genome editing technologies specifically could result in additional regulations restricting or prohibiting our products. Even if any product candidates we may develop receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors, and others in the medical community. The degree of market acceptance of any product candidates we may develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in clinical trials;
- the potential and perceived advantages compared to alternative treatments;
- the limitation to our targeted patient population and limitations or warnings contained in approved labeling by the FDA or other regulatory authority;
- the ability to offer our medicines for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the clinical indications for which the product candidate is approved by FDA, the European Commission, or other regulatory agencies;
- public attitudes regarding genomic medicine generally and genome editing technologies specifically;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, as well as their willingness to accept a therapeutic intervention that involves the editing of the patient's genome;
- product labeling or product insert requirements of the FDA, the EMA, or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- relative convenience and ease of administration;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and

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- the prevalence and severity of any side effects.

If any product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues, and we may not become profitable.

***If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved.***

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing, or distribution of pharmaceutical products. To achieve commercial success for any approved medicine for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support 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 commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists 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 and other commercialization 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 commercialization personnel.

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

- our inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs, and other support personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future medicines;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- the lack of complementary medicines 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 commercialization organization.

If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our product revenues or the profitability of these product revenues to us may be lower than if we were to market and sell any medicines we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may 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 medicines effectively. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.



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***We face significant competition in an environment of rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any product candidates we may develop.***

The development and commercialization of new drug products is highly competitive. Moreover, the genome editing field is characterized by rapidly changing technologies, significant competition, and a strong emphasis on intellectual property. We will face competition with respect to any product candidates that we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we have research programs, including LCA10, Duchenne muscular dystrophy, and cystic fibrosis. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches.

Our platform and product focus is the development of therapies using CRISPR technology. Companies developing CRISPR technology include Caribou Biosciences, CRISPR Therapeutics, ERS Genomics, Intellia Therapeutics, and TRACR Hematology. There are additional companies developing therapies using additional genome editing technologies, including transcription activator-like effector nucleases, meganucleases, Mega-TALs, and zinc finger nucleases. These companies include bluebird bio, Cellectis, Poseida Therapeutics, Precision Biosciences, and Sangamo Therapeutics. Additional companies developing gene therapy products include Abeona Therapeutics, Adverum Biotechnologies, AGTC Therapeutics, Dimension Therapeutics, REGENXBIO, Spark Therapeutics, uniQure, and Voyager Therapeutics. In addition to competition from other genome editing therapies or gene therapies, any products we may develop may also face competition from other types of therapies, such as small molecule, antibody, or protein therapies.

Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology, and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop or that would render any products that we may develop obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

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***Even if we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices, or healthcare reform initiatives, which would harm our business.***

The regulations that govern marketing approvals, pricing, and reimbursement for new medicines vary widely from country to country. In the United States, recently enacted legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a medicine before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a medicine in a particular country, but then be subject to price regulations that delay our commercial launch of the medicine, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the medicine in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

Our ability to commercialize any medicines successfully also will depend in part on the extent to which reimbursement for these medicines and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any medicine that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved medicines, and coverage may be more limited than the purposes for which the medicine is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any medicine will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new medicines, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the medicine and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost medicines and may be incorporated into existing payments for other services. Net prices for medicines may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of medicines from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved medicines we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize medicines, and our overall financial condition.

***Due to the novel nature of our technology and the potential for any product candidates we may develop to offer therapeutic benefit in a single administration or limited number of administrations, we face uncertainty related to pricing and reimbursement for these product candidates.***

Our initial target patient populations are relatively small, as a result of which the pricing and reimbursement of any product candidates we may develop, if approved, must be adequate to support the necessary commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any such product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to any product candidates we may develop (e.g., for administration of our product to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability

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to market or sell our products. In addition, it may be necessary for us to develop new reimbursement models in order to realize adequate value. Payors may not be able or willing to adopt such new models, and patients may be unable to afford that portion of the cost that such models may require them to bear. If we determine such new models are necessary but we are unsuccessful in developing them, or if such models are not adopted by payors, our business, financial condition, results of operations, and prospects could be adversely affected.

We expect the cost of a single administration of genomic medicine products, such as those we are seeking to develop, to be substantial, when and if they achieve regulatory approval. We expect that coverage and reimbursement by government and private payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of any such product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of any product candidates we may develop will be paid by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or will be reimbursed by government authorities, private health coverage insurers, and other third-party payors. Coverage and reimbursement by a third-party payor may depend upon several 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.

Obtaining coverage and reimbursement for a product from third-party payors is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical, and cost-effectiveness data. There is significant uncertainty related to third-party coverage and reimbursement of newly approved products. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize any product candidates we may develop. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment.

Moreover, the downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products such as ours. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any product candidates we may develop will be harmed.

***If the market opportunities for any product candidates we may develop are smaller than we believe they are, our revenues may be adversely affected, and our business may suffer. Because the target patient populations for many of the product candidates we may develop are small, we must be able to successfully identify patients and achieve a significant market share to maintain profitability and growth.***

We focus our research and product development on treatments for rare genetically defined diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with product candidates we may develop, are based on estimates. These estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of these diseases. The number of patients in the United States, Europe, and elsewhere may turn out to be lower than expected, and patients may not be amenable to treatment with our products, or may become increasingly difficult to identify or gain access to, all of which would adversely affect our business, financial condition, results of operations, and prospects.

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### ***Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any medicines that we may develop.***

We face an inherent risk of product liability exposure related to the testing in human clinical trials of any product candidates we may develop and will face an even greater risk if we commercially sell any medicines that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or medicines caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or medicines that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant time and costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any medicines that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage when we begin clinical trials and if we successfully commercialize any medicine. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

### ***If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.***

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research and product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. 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 carry specific biological or hazardous waste insurance coverage, and our commercial general liability and umbrella liability policies (under which we currently have an aggregate of \$7.0 million in coverage) specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized

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with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, we may incur substantial costs in order to comply with current or future environmental, health, and safety laws, regulations, and permitting requirements. These current or future laws, regulations, and permitting requirements may impair our research, development, or production efforts. Failure to comply with these laws, regulations, and permitting requirements also may result in substantial fines, penalties, or other sanctions or business disruption, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Any third-party contract manufacturers and suppliers we engage will also be subject to these and other environmental, health, and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***Genomic medicines are novel, and any product candidates we develop may be complex and difficult to manufacture. We could experience production problems that result in delays in our development or commercialization programs, limit the supply of our products, or otherwise harm our business.***

Any product candidates we may develop will likely require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as the product candidates we intend to develop 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. 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. If we successfully develop product candidates, we may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other comparable applicable foreign standards or specifications with consistent and acceptable production yields and costs. To date, we are not aware of any cGMP gene therapy manufacturing facility in the United States receiving approval from the FDA for the manufacture of an approved genome editing or gene therapy product, and, therefore, the timeframe required for us to obtain such approval is uncertain.

In addition, the FDA, the EMA, and other 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 regulatory authorities may require that we not distribute a lot until the 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 clinical trials or product launches, which could be costly to us and otherwise harm our business, financial condition, results of operations, and prospects.

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

Given the nature of biologics manufacturing, there is a risk of contamination during manufacturing. Any contamination could materially harm our ability to produce product candidates on schedule and could harm our results of operations and cause reputational damage. Some of the raw materials that we anticipate will be required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall, or restriction on the use of biologically derived substances in the manufacture of any product candidates we may develop could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially harm our development timelines and our business, financial condition, results of operations, and prospects.

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Any problems in our manufacturing process or the facilities with which we contract 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. Problems in third-party manufacturing process or facilities also could restrict our ability to meet market demand for any products we develop and commercialize.

### **Risks Related to Our Dependence on Third Parties**

*We expect to depend on collaborations with third parties for the research, development, and commercialization of certain of the product candidates we may develop or for development of certain of our research programs. If any such collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates or research programs.*

We anticipate seeking third-party collaborators for the research, development, and commercialization of certain of the product candidates we may develop or for development of certain of our research programs. For example, in May 2015, we entered into a collaboration with Juno Therapeutics focused on research and development of engineered T cell immunotherapies that utilize or incorporate our genome editing technologies. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, and biotechnology companies. If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of any product candidates we may seek to develop with them. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs or any product candidates we may develop, including our collaboration with Juno Therapeutics, pose the following risks to us:

- Collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations. For example, under our collaboration with Juno Therapeutics, development and commercialization plans and strategies for licensed programs will be conducted in accordance with a plan and budget approved by a joint research committee, or JRC, comprised of equal numbers of representatives from each of us and Juno Therapeutics.
- Collaborators may not pursue development and commercialization of any product candidates we may develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities. For example, it is possible for Juno Therapeutics to elect not to submit an IND for a product candidate that we have nominated and the JRC confirmed without triggering a termination of the collaboration arrangement.
- 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 medicines or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.
- Collaborators with marketing and distribution rights to one or more medicines may not commit sufficient resources to the marketing and distribution of such medicine or medicines.
- Collaborators may not properly obtain, maintain, enforce, or defend our intellectual property or proprietary rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation. For example, Juno Therapeutics has the first right to enforce or defend certain of our intellectual property rights under our collaboration

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arrangement with respect to certain licensed programs, and although we may have the right to assume the enforcement and defense of such intellectual property rights if Juno Therapeutics does not, our ability to do so may be compromised by Juno Therapeutics' actions.

- Disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our medicines or product candidates or that result in costly litigation or arbitration that diverts management attention and resources.
- We may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control.
- Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates. For example, Juno Therapeutics can terminate its agreement with us in its entirety upon six months' notice and can terminate the entire agreement with us in connection with a material breach of the agreement by us that remains uncured for a specified period of time.
- Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished, or terminated.

If our collaborations do not result in the successful 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 product candidates could be delayed, and we may need additional resources to develop product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval, and commercialization described in this Annual Report on Form 10-K apply to the activities of our collaborators.

We may in the future decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of any product candidates we may develop. These relationships, or those like them, may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement 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 several factors. If we license rights to any product candidates we or our collaborators may develop, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

***If we are not able to establish collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.***

Our product development and research programs and the potential commercialization of any product candidates we may develop will require substantial additional cash to fund expenses. For some of the product candidates we may develop or certain of our research programs, we may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates or programs.

We face significant competition in seeking appropriate collaborators. Whether we 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



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factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. For example, during the research program term of our collaboration with Juno Therapeutics, we may not directly or indirectly license, fund, enable, or participate in any research, development, manufacture, or commercialization of engineered T cells with chimeric antigen receptors and T cell receptors in the field of diagnosis, treatment, or prevention of cancer in humans through the use of engineered T cells, excluding the diagnosis, treatment, or prevention of medullary cystic kidney disease.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, 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 increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

***We expect to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research, or testing.***

We expect to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct our clinical trials. We currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical testing. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practices, for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates we may develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines.

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We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of any product candidates we may develop or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

***We contract with third parties for the manufacture of materials for our research programs and preclinical studies and expect to continue to do so for clinical trials and for commercialization of any product candidates that we may develop. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.***

We do not have any manufacturing facilities. We currently rely on third-party manufacturers for the manufacture of our materials for preclinical studies and expect to continue to do so for clinical testing and for commercial supply of any product candidates that we may develop and for which we or our collaborators obtain marketing approval. We do not have a long term supply agreement with any of the third-party manufacturers, and we purchase our required supply on a purchase order basis.

We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business, financial condition, results of operations, and prospects.

Any medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for bulk drug substances. If any one of our current contract manufacturer cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there are several potential alternative manufacturers who could manufacture any product candidates we may develop, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of any product candidates we may develop or medicines may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

## Risks Related to Our Intellectual Property

***If we are unable to obtain and maintain patent protection for any products we develop and for our technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop, and our technology may be adversely affected.***

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our CRISPR platform technology and any proprietary product candidates and technology we develop. We seek to protect our proprietary position by in-licensing intellectual property relating to our platform technology and filing patent applications in the United States and abroad related to our technologies and product candidates that are important to our business. If we or our licensors are unable to obtain or maintain patent protection with respect to our CRISPR platform technology and any proprietary products and technology we develop, our business, financial condition, results of operations, and prospects could be materially harmed.

No consistent policy regarding the scope of claims allowable in the field of genome editing, including CRISPR technology, has emerged in the United States. The scope of patent protection outside of the United States is also uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. With respect to both in-licensed and owned intellectual property, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, 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 cannot be certain that we were the first to make the inventions claimed in our owned or any licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we license or own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we hold or in-license may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether any of our platform advances and product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. For example, we are aware that third parties have suggested the use of the CRISPR technology in conjunction with a protein other than Cas9 or Cpf1. Our owned and in-licensed patents may not cover CRISPR technology in conjunction with a protein other than Cas9 or Cpf1. If our

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competitors commercialize the CRISPR technology in conjunction with a protein other than Cas9 or Cpf1, our business, financial condition, results of operations, and prospects could be materially adversely affected.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Our licensors are currently, and we or our licensors may in the future become, subject to a third party pre-issuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or opposition, derivation, revocation, re-examination, post-grant and *inter partes* review, or interference proceedings and other similar proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, we, or one of our licensors, may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of patentability. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, 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 product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. As discussed below, some of our in-licensed patents are subject to inventorship disputes and interference, opposition, and *ex parte* re-examination proceedings and therefore subject to these risks.

In addition, 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 intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Moreover, some of our owned and in-licensed patents and patent applications are, and may in the future be, co-owned with third parties. If we are unable to obtain an exclusive license to any such third party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we or our licensors may need the cooperation of any such co-owners of our owned and in-licensed patents in order to enforce such patents against third parties, and such cooperation may not be provided to us or our licensors. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Furthermore, our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties. For example, the research resulting in certain of our owned and in-licensed patent rights and technology was funded in part by the U.S. government. As a result, the U.S. government has certain rights, including march-in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention. For example, our licensors, including The Broad Institute, Inc., or Broad, have granted the U.S. government a non-exclusive, non-transferable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States, the inventions described in certain of our in-licensed patents and patent applications, including certain aspects of our in-licensed CRISPR technology. If the government decides to exercise these rights, it is not required to engage us as its contractor in connection with doing so. These rights may permit the U.S. government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The U.S. government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of any of the foregoing rights could harm our competitive position, business, financial condition, results of operations, and prospects.

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***Our rights to develop and commercialize our technology and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.***

We are heavily reliant upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our genome editing technology, including our CRISPR technology, and product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses. For example, pursuant to our license agreements with Broad and the President and Fellows of Harvard College, or Harvard, the licensors may, under certain circumstances, grant a license to the patents that are the subject of such license agreements to a third party. Such third party would have full rights to the patent rights that are the subject of such licenses, which could impact our competitive position and enable a third party to commercialize products similar to our future product candidates and technology. Furthermore, under these license agreements, Broad has the right, after specified periods of time and subject to certain limitations, to designate gene targets for which Broad, whether alone or together with an affiliate or third party, has an interest in researching and developing products that would otherwise be covered by rights licensed to us under the agreements. Any of the foregoing would narrow the scope of our exclusive rights to the patents and patent applications we have in-licensed from Broad. The terms of these license agreements are described more fully under “Business—License Agreements”. In addition, our rights to our in-licensed patents and patent applications are dependent, in part, on inter-institutional or other operating agreements between the joint owners of such in-licensed patents and patent applications. If one or more of such joint owners breaches such inter-institutional or operating agreements, our rights to such in-licensed patents and patent applications may be adversely affected, which could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

In addition, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. For example, pursuant to each of our intellectual property licenses with Broad, Harvard, The General Hospital Corporation, d/b/a Massachusetts General Hospital and Duke University, our licensors retain control of preparation, filing, prosecution, and maintenance, and, in certain circumstances, enforcement and defense of their patents and patent applications. Therefore, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our products that are subject of such licensed rights could be adversely affected. Additionally, given that we are required to reimburse our licensors for all of their expenses related to the prosecution, maintenance, enforcement and defense of patents and patent applications that we in-license from them, the ongoing nature of the inventorship disputes and the interference, opposition, and re-examination proceedings involving the patents licensed to us under our license agreement with Harvard and Broad and our obligation to make such reimbursements are not subject to any limitations, we anticipate that our obligation to reimburse our licensors for expenses related to these matters will continue to be substantial. During the years ended December 31, 2014, 2015, and 2016 we paid an aggregate of \$1.7 million, \$9.4 million, and \$23.6 million in connection with these reimbursement obligations.

Our licensors may have relied on third party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents we in-licensed. For example, certain patent applications licensed to us by Broad are co-owned with NIH. Broad does not and does not purport to grant any rights in NIH’s interest in these patent applications under our agreement. If other third parties have ownership rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory

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approval of, and to market, products identical to ours. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties (potentially including our competitors) to receive licenses to a portion of the intellectual property that is subject to our existing licenses. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

***Some of our in-licensed patents are subject to inventorship, priority, and validity disputes. In addition, our owned and in-licensed patents and other intellectual property may be subject to further inventorship, priority and validity disputes, and other similar intellectual property proceedings. If we or our licensors are unsuccessful in any of these proceedings, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms or at all, or to cease the development, manufacture, and commercialization of one or more of the product candidates we may develop, which could have a material adverse impact on our business.***

On January 11, 2016, the Patent Trial and Appeal Board of the USPTO, or PTAB, declared an interference between a pending U.S. patent application (U.S. Serial No. 13/842,859) that is owned by the University of California, the University of Vienna, and Emmanuelle Charpentier and 12 U.S. patents (U.S. Patent Nos. 8,697,359; 8,771,945; 8,795,965; 8,865,406; 8,871,445; 8,889,356; 8,895,308; 8,906,616; 8,932,814; 8,945,839; 8,993,233; and 8,999,641) that are co-owned by Broad and MIT, and in some cases Harvard, and in-licensed by us. On March 17, 2016, the PTAB re-declared the interference to add a pending U.S. patent application (U.S. Serial No. 14/704,551) that is co-owned by Broad, MIT, and Harvard, and in-licensed by us. An interference is a proceeding within the USPTO to determine priority of invention of the subject matter of patent claims filed by different parties. This proceeding is only potentially available for patent applications filed in the United States on or before March 15, 2013 and related continuing patent applications. In the interference, the University of California, the University of Vienna and Emmanuelle Charpentier asserted that inventors from the University of California and the University of Vienna, and Emmanuelle Charpentier made certain inventions claimed in the Broad, MIT and Harvard patents before the inventors from Broad, MIT and, in certain cases, Harvard.

In the declared interference, the University of California, acting on behalf of itself and the University of Vienna, and Emmanuelle Charpentier were designated as the senior party and Broad was designated as the junior party. In an interference proceeding, the junior party has the burden of proof and presents its priority evidence first. The declaration of interference defined the invention that is subject to the declaration of interference, also referred to as “the count,” as relating to a method that involves contacting a target DNA in a eukaryotic cell with certain defined CRISPR/Cas9 components for the purpose of cleaving or editing a target DNA molecule or modulating transcription of at least one gene encoded thereon. All of the claims in the pending U.S. patent application that is owned by the University of California, the University of Vienna, and Emmanuelle Charpentier and all of the claims in the 12 U.S. patents and one pending U.S. patent application that are co-owned by Broad and MIT, and in some cases Harvard, and in-licensed by us were implicated in the interference. The University of California, the University of Vienna, and Emmanuelle Charpentier are listed as applicants on U.S. Serial No. 13/842,859. The University of California derives rights in U.S. Serial No. 13/842,859 from an assignment by Dr. Jennifer Doudna and certain other inventors listed on such application. Caribou Biosciences has reported that it has an exclusive license to patent rights from the University of California and the University of Vienna. Intellia Therapeutics has reported that it has an exclusive license to such rights from Caribou Biosciences in certain fields. CRISPR Therapeutics, ERS Genomics, and TRACR Hematology, also our competitors, have reported that they have exclusively licensed such patent rights from Emmanuelle Charpentier. Further, Dr. Doudna was a founder of our company and entered into a consulting agreement with us at the time of our founding. However, Dr. Doudna gave notice of termination of that agreement in May 2014 after less than seven months of service, and she has had no further engagement in our business since that time. Dr. Doudna is also a founder of Caribou Biosciences and has been publicly identified as an advisor to Intellia Therapeutics, each of which is one of our competitors.

As a result of the declaration of interference, an adversarial proceeding in the USPTO before the PTAB was initiated. An interference is declared to ultimately determine priority, specifically which party was first to invent the commonly claimed invention. An interference is typically divided into two phases. The first phase is typically referred to as the motions or preliminary motions phase while the second is referred to as the priority phase. In the first phase, each party may raise issues including but not limited to those relating to the patentability of a party’s claims based on prior



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art, written description, and enablement. A party also may seek an earlier priority benefit or may challenge whether the declaration of interference was proper in the first place. Priority, or a determination of who first invented the commonly claimed invention, is determined in the second phase of an interference.

On February 15, 2017, the PTAB held that there is no interference-in-fact between the parties for the subject matter of the count. A judgment of no interference-in-fact means that no interference is needed to resolve priority between the parties because the PTAB determined that our in-licensed claims are directed to subject matter that is patentably distinct from those of the University of California, the University of Vienna, and Emmanuelle Charpentier. The interference proceeding has therefore ended without reaching the second priority phase. Therefore, the 12 U.S. patents and one U.S. patent application that we have in-licensed from Broad, acting on behalf of itself, MIT, and Harvard, as well as the U.S. patent application owned by the University of California, the University of Vienna, and Emmanuelle Charpentier, with respect to which the PTAB had declared an interference were not modified or revoked as a result of this interference proceeding. However, the University of California, the University of Vienna, and Emmanuelle Charpentier may request a rehearing of the judgment by the PTAB within 30 days and/or may appeal to the Court of Appeals for the Federal Circuit, or the Federal Circuit, within 63 days. It is uncertain when and in what manner the PTAB or Federal Circuit would act on such a request for rehearing or appeal. A final, non-appealable judgment of no interference-in-fact bars any further interference between the same parties for claims to the same invention as the count of the interference. However, as discussed below, certain of these 12 U.S. patents and one U.S. patent application are, or may in the future be, subject to further intellectual property proceedings and disputes, including interference proceedings.

The University of California, the University of Vienna, and Emmanuelle Charpentier or other third parties may file a separate Suggestion of Interference against the Broad patents that were subject to the interference or other U.S. patents and patent applications that we own or in-license. For example, ToolGen Inc., or ToolGen, filed Suggestions of Interference in the USPTO on April 13, 2015, which became publicly available on November 12, 2015 and December 3, 2015, suggesting that they believe some of the claims in pending U.S. applications owned by ToolGen (U.S. Serial No. 14/685,568 and U.S. Serial No. 14/685,510, respectively) interfere with certain claims in five U.S. patents, which we have in-licensed from Broad, acting on behalf of itself, MIT, and Harvard. These five U.S. patents are among the 12 U.S. patents with respect to which the PTAB had declared an interference with the pending U.S. patent application (U.S. Serial No. 13/842,859) that is owned by the University of California, the University of Vienna, and Emmanuelle Charpentier. The Suggestions of Interference that were filed by ToolGen are still pending and it is uncertain when and in what manner the USPTO will act on them.

Our owned and in-licensed patents and patent applications are, and may in the future become, subject to validity disputes in the USPTO and other foreign patent offices. A request for *ex parte* re-examination was filed with the USPTO on February 16, 2016 against one patent that we have in-licensed from Broad, acting on behalf of itself and MIT (U.S. Patent No. 8,771,945), which was subject to the interference proceeding involving the University of California, the University of Vienna, and Emmanuelle Charpentier and referenced in the Suggestions of Interference filed by ToolGen. *Ex parte* re-examination is a procedure through which a third party can anonymously request the USPTO to re-examine a granted patent because the third party believes the granted patent may not be patentable over prior art in the form of a printed publication or another patent. Before the USPTO will re-examine a granted patent, the third party requestor must establish that the submitted prior art establishes a substantial and new question of patentability. If the USPTO determines there is a substantial and new question of patentability, it grants the re-examination request and re-examines the patent after giving the patent owner the option of filing an initial statement. The request for *ex parte* re-examination of U.S. Patent No. 8,771,945 was granted on May 9, 2016 thereby initiating a re-examination procedure between the USPTO and Broad, acting on behalf of itself and MIT. The third party requestor does not participate in the re-examination procedure after filing the request except that it has the option of responding if the patent owner chooses to file an initial statement. On May 12, 2016, the PTAB suspended the re-examination of U.S. Patent No. 8,771,945 noting that it has jurisdiction over any file that involves a patent involved in the interference. It is uncertain when the PTAB will lift the suspension, however the PTAB may do so in light of the PTAB's no interference-in-fact holding. If Broad is unsuccessful during the re-examination, U.S. Patent No. 8,771,945 may be revoked or narrowed, which could have a material adverse effect on the scope of our rights under such patent.



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The 12 in-licensed U.S. patents and one in-licensed U.S. patent application that were the subject of the interference with the pending U.S. patent application (U.S. Serial No. 13/842,859) that is owned by the University of California, the University of Vienna, and Emmanuelle Charpentier (which includes the five in-licensed U.S. patents that are the subject of the Suggestions of Interference filed by ToolGen and the one in-licensed U.S. patent that is the subject of the re-examination) relate generally to the CRISPR/Cas9 system and its use in eukaryotic cells. The claims of the 12 in-licensed U.S. patents and one in-licensed U.S. patent application vary in scope and coverage and include claims that are directed to CRISPR/Cas9 systems that employ viral vectors for delivery, single guide RNAs, modified guide RNAs, *S. aureus* Cas9, or a Cas9 nickase and are relevant to our genome editing platform technology. The loss or narrowing in scope of one or more of these in-licensed patents could have a material adverse effect on the conduct of our business, financial condition, results of operations, and prospects. The loss or narrowing in scope of one or more of these in-licensed patents could have a material adverse effect on the conduct of our business.

In addition, we or our licensors may be subject to claims that former employees, collaborators, or other third parties have an interest in our owned or in-licensed patents or patent applications, or other intellectual property as an inventor or co-inventor. If we are unable to obtain an exclusive license to any such third party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors. In addition, we may need the cooperation of any such co-owners to enforce any patents, including any patents that issue from such patent applications, against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on the conduct of our business, financial condition, results of operations, and prospects.

We or our licensors are subject to and may in the future become a party to similar proceedings or priority disputes in Europe or other foreign jurisdictions. The European Patent Office Opposition Division has initiated opposition proceedings in the European Patent Office, or EPO, against four European patents that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard (European Patent Nos. EP 2,771,468 B1, EP 2,784,162 B1, EP 2,896,697 B1 and EP 2,931,898 B1) and one European patent that we have in-licensed from Broad, acting on behalf of itself and MIT (European Patent No. EP 2,764,103 B1). The EPO opposition proceedings may involve issues including, but not limited to, procedural formalities related to filing the European patent application, priority, and the patentability of the involved claims. One or more of the third parties that have filed oppositions against European Patent Nos. EP 2,771,468 B1, EP 2,784,162 B1, EP 2,764,103 B1, EP 2,896,697 B1, and/or EP 2,931,898 B1 or other third parties may file future oppositions against other European patents that we in-license or own. For example, we are aware that oppositions have been filed against two other European patents that we in-license from Broad, acting on behalf of itself, MIT and Harvard (European Patent Nos. EP 2,898,075 B1 and EP 2,921,557 B1). The deadline for filing oppositions against the second of these European patents is April 13, 2017. There may be other oppositions against this European patent that have not yet been filed or that have not yet been made available to the public. In addition, we are aware that Intellia Therapeutics has filed petitions in two actions in United States District Court seeking discovery of information, including inventorship information, related to issues in these pending EPO opposition proceedings. Disclosure of any such information may result in additional validity challenges to our in-licensed European patents and patent applications. The loss of priority for, or the loss of, these European patents could have a material adverse effect on the conduct of our business.

If we or our licensors are unsuccessful in any patent related disputes, including interference proceedings, patent oppositions, reexaminations, or other priority, inventorship, or validity disputes to which we or they are subject (including any of the proceedings discussed above), we may lose valuable intellectual property rights through the loss of one or more patents owned or licensed or our owned or licensed patent claims may be narrowed, invalidated, or held unenforceable. In addition, if we or our licensors are unsuccessful in any inventorship disputes to which we or they are subject, we may lose valuable intellectual property rights, such as exclusive ownership of, or the exclusive right to use, our owned or in-licensed patents. If we or our licensors are unsuccessful in any interference proceeding or other priority or inventorship dispute, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other priority or inventorship disputes. Such licenses may not be available on commercially reasonable terms or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture, and commercialization of one or more of the product candidates we may develop. The loss of exclusivity or the narrowing of our owned and licensed patent claims could limit our ability to stop others from using or commercializing similar or identical technology and products. Any of the foregoing could

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result in a material adverse effect on our business, financial condition, results of operations, or prospects. Even if we are successful in any interference proceeding or other priority, inventorship, or validity disputes, it could result in substantial costs and be a distraction to our management and other employees.

### ***We may not be able to protect our intellectual property and proprietary rights throughout the world.***

Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. In addition, our intellectual property license agreements may not always include worldwide rights. For example, certain U.S. patent applications licensed to us by Broad include The University of Tokyo, or Tokyo, and NIH as joint applicants. Broad has only granted a license to us with respect to its interests and to Tokyo's interests in these U.S. patent applications but not to any foreign equivalents thereof. 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 or licenses but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims 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 and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

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

Periodic maintenance fees, renewal fees, annuity fees, and various other government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned or licensed patents and applications. In certain circumstances, we rely on our licensing partners to pay these fees due to U.S. and non-U.S. patent agencies. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. We are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market

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with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.***

We have entered into license agreements with third parties and may need to obtain additional licenses from our existing licensors and others to advance our research or allow commercialization of product candidates we may develop. It is possible that we may be unable to obtain any additional licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third party patents do not exist which might be enforced against our current technology, including CRISPR genome editing technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

In each of our license agreements, and we expect in our future agreements, we are responsible for bringing any actions against any third party for infringing on the patents we have licensed. Certain of our license agreements also require us to meet development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

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### ***We may not be successful in obtaining necessary rights to any product candidates we may develop through acquisitions and in-licenses.***

We currently have rights to intellectual property, through licenses from third parties, to identify and develop product candidates. Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us in the field of genome editing technology and filing patent applications potentially relevant to our business. For example, we are aware of several third party patent applications that, if issued, may be construed to cover our CRISPR technology and product candidates. In order to avoid infringing these third party patents, we may find it necessary or prudent to obtain licenses from such third party intellectual property holders. We may also require licenses from third parties for certain non-CRISPR technologies including certain delivery methods that we are evaluating for use with product candidates we may develop. In addition, with respect to any patents we co-own with third parties, we may require licenses to such co-owners' interest to such patents. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for product candidates we may develop and CRISPR technology. The licensing or acquisition of third party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. For example, certain delivery modes, including certain adeno-associated virus vectors and lipid nanoparticle technologies, we are evaluating for use in our LCA10 program or with other product candidates we may develop are covered by patents held by third parties. If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

### ***Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.***

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or America Invents Act, enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

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### ***Issued patents covering our technology and product candidates could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad.***

If we or one of our licensors initiated legal proceedings against a third party to enforce a patent covering a product candidate we may develop or our technology, including CRISPR genome editing technology, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties have raised challenges to the validity of certain of our in-licensed patent claims and may in the future raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). For example, as discussed above, an interference was declared, and multiple Suggestions of Interference have been filed against certain of our in-licensed U.S. patents and patent applications, one of these U.S. patents is subject to a re-examination proceeding, opposition proceedings have been initiated against five of our in-licensed European patents, oppositions have been filed against another two of our in-licensed European patents, and additional interference, re-examination, opposition, and other intellectual property proceedings may be initiated in the future. For more information regarding these proceedings, see “Legal Proceedings” in Part I, Item 3 of this Annual Report on Form 10-K. Such proceedings could result in the revocation of, cancellation of, or amendment to our patents in such a way that they no longer cover our technology or platform, or any product candidates that we may develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we or our licensing partners and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology or platform, or any product candidates that we may develop. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and prospects.

### ***The intellectual property landscape around genome editing technology, including CRISPR, is highly dynamic, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.***

The field of genome editing, especially in the area of CRISPR technology, is still in its infancy, and no such products have reached the market. Due to the intense research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is in flux, and it may remain uncertain for the coming years. There may be significant intellectual property related litigation and proceedings relating to our owned and in-licensed, and other third party, intellectual property and proprietary rights in the future.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market, and sell any product candidates that we may develop and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. We are subject to and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and any product candidates we may develop, including interference proceedings, post-grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the EPO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. We are aware of certain third party patent applications in this landscape that may, if issued as patents, be asserted to encompass our CRISPR/Cas9 technology. In particular, we are aware of several separate families of U.S. patent applications and foreign counterparts which relate to CRISPR/Cas9 technology, where the earliest priority dates of each family pre-date the priority dates of our in-licensed patents and patent applications, including PCT Publication No. WO 2013/176772 (and its related U.S. patent applications and foreign counterparts) filed by the

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University of California, the University of Vienna (both of which are reported to have exclusively licensed their rights to Caribou Biosciences, which is reported to have exclusively licensed certain rights to Intellia Therapeutics), and Emmanuelle Charpentier (who is reported to have exclusively licensed her rights to CRISPR Therapeutics, ERS Genomics and TRACR Hematology), and WO 2014/065596 (and its related U.S. patent applications and foreign counterparts) filed by ToolGen. Each of these patent families are owned by a different third party and contain claims that may be construed to cover components and uses of CRISPR/Cas9 technology. If we are not able to obtain or maintain a license on commercially reasonable terms to any third-party patents that cover our product candidates or activities, such third parties could potentially assert infringement claims against us, which could have a material adverse effect on the conduct of our business. We are also aware of third-party U.S. patents (U.S. Patent No. 8,921,332 and U.S. Patent No. 9,458,439), which are reported to have been exclusively licensed to Cellectis and contain claims related to methods for inducing double strand breaks in chromosomal DNA using a chimeric restriction endonuclease. In addition, we are aware of a U.S. patent and a related U.S. continuation patent application (U.S. Patent No. 9,200,266 and U.S. Serial No. 14/925,386) that is assigned to Sangamo Biosciences, Inc. and contains claims to a chimeric nuclease that induces a site-specific single-stranded break in a double-stranded DNA. Although we believe that we do not infringe a valid claim of such third party patents, such third parties may assert infringement claims or claim infringement against us, and if we are found to infringe such third party patents, we may be required to pay damages, cease commercialization of the infringing technology, or obtain a license from such third parties, which may not be available on commercially reasonable terms or at all.

Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, or priority. A court of competent jurisdiction could hold that these third party patents are valid, enforceable, and infringed, which could materially and adversely affect our ability to commercialize any product candidates we may develop and any other product candidates or technologies covered by the asserted third party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe a third party's intellectual property rights, and we are unsuccessful in demonstrating that such patents are invalid or unenforceable, we could be required to obtain a license from such third party to continue developing, manufacturing, and marketing any product candidates we may develop and our 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 and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We also could be forced, including by court order, to cease developing, manufacturing, and commercializing the infringing technology or product candidates. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations, and prospects.

***We may be subject to claims that our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.***

Many of our employees, consultants, and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we



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may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming, and unsuccessful.***

Competitors may infringe our patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. In addition, our patents or the patents of our licensing partners also are, and may in the future become, involved in inventorship, priority, or validity disputes. To counter or defend against such claims can be expensive and time consuming. In an infringement proceeding, a court may decide that a patent owned or in-licensed by us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our owned and in-licensed patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly. 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.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and 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. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

***If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.***

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information and to maintain our competitive position. With respect to our technology platform, we consider trade secrets and know-how to be one of our primary sources of intellectual property. Trade secrets and know-how can be difficult to protect. In particular, we anticipate that with respect to our technology platform, these trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel from academic to industry scientific positions.

We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from



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using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

***If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.***

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

***Intellectual property rights do not necessarily address all potential threats.***

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make gene therapy products that are similar to any product candidates we may develop or utilize similar gene therapy technology but that are not covered by the claims of the patents that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending licensed patent applications or those that we may own in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;

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- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects.

### **Risks Related to Regulatory Approval and Other Legal Compliance Matters**

***Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming, and uncertain and may prevent us from obtaining approvals for the commercialization of any product candidates we may develop. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, product candidates we may develop, and our ability to generate revenue will be materially impaired.***

Any product candidates we may develop and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the biologic product candidate's safety, purity, and potency. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any product candidates we develop may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical, or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved medicine not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of any product candidates we may develop, the commercial prospects for those product candidates may be harmed, and our ability to generate revenues will be materially impaired.

***Failure to obtain marketing approval in foreign jurisdictions would prevent any product candidates we may develop from being marketed in such jurisdictions, which, in turn, would materially impair our ability to generate revenue.***

In order to market and sell any product candidates we may develop in the European Union and many other foreign jurisdictions, we or our third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA

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approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our medicines in any jurisdiction, which would materially impair our ability to generate revenue.

***Even if we, or any collaborators we may have, obtain marketing approvals for any product candidates we develop, the terms of approvals and ongoing regulation of our products could require the substantial expenditure of resources and may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.***

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising, and promotional activities for such medicine, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the medicine may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine.

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more product candidates we develop, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, and quality control. If we and such collaborators are not able to comply with post-approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition, and prospects.

***Any product candidate for which we obtain marketing approval could be subject to restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our medicines, when and if any of them are approved.***

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of medicines to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our medicines for their approved indications, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice. Violation of the Federal Food, Product, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown problems with our medicines, manufacturers, or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such medicines, manufacturers, or manufacturing processes;
- restrictions on the labeling or marketing of a medicine;

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- restrictions on the distribution or use of a medicine;
- requirements to conduct post-marketing clinical trials;
- receipt of warning or untitled letters;
- withdrawal of the medicines from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of medicines;
- fines, restitution, or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our medicines;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize any product candidates we may develop and adversely affect our business, financial condition, results of operations, and prospects.

***Our relationships with healthcare providers, physicians, and third-party payors will be subject to applicable anti-kickback, fraud and abuse, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, and diminished profits and future earnings.***

Healthcare providers, physicians, and third-party payors play a primary role in the recommendation and prescription of any product candidates that we may develop for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving, or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order, or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid, or other government payors that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at \$5,500 to \$11,000 per false claim;

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- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as further amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, which imposes certain requirements, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, health care clearinghouses, and health care providers;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services;
- the federal transparency requirements under the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics, and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

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. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization, and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

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 authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs. Liabilities they incur

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pursuant to these laws could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

***Future legislation, and any changes to existing legislation, may increase the difficulty and cost for us and any collaborators we may have to obtain marketing approval of and commercialize any product candidates we may develop and affect the prices we, or they, may obtain.***

In the United States and some foreign jurisdictions, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of any product candidates that we may develop, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or our future collaborators, may receive for any approved products.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

The Patient Protection and Affordable Care Act enacted in March 2010 and subsequently amended by the Health Care and Education Affordability Reconciliation Act, or collectively, PPACA, contains several provisions of potential importance to any product candidates we may develop, including the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription products and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Product Rebate Program;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for non-compliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report product samples that manufacturers and distributors provide to physicians; and

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- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any product candidates we may develop for which marketing approval is obtained.

We expect that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue from sales of products, attain profitability, or commercialize any product candidates we may develop.

In addition, with the new Presidential Administration and Congress, there will likely be additional legislative changes, including repeal and replacement of certain provisions of the PPACA. It remains to be seen, however, precisely what the new legislation will provide, when it will be enacted and what impact it will have on the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop product candidates.

Moreover, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our drug candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and our future collaborators to more stringent drug labeling and post-marketing testing and other requirements.

***Fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process, and does not assure FDA approval of our product candidates.***

If a product candidate is intended for the treatment of a serious or life threatening condition and the product candidate demonstrates the potential to address unmet medical need for this condition, the sponsor may apply for FDA fast track designation. However, a fast track designation does not ensure that the product candidate will receive marketing approval or that approval will be granted within any particular timeframe. As a result, while we may seek and receive fast track designation for our product candidates, we may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

***Priority review designation by the FDA may not lead to a faster regulatory review or approval process and, in any event, does not assure FDA approval of our product candidates.***

If the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for certain of our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or thereafter.



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***We may not be able to obtain orphan drug exclusivity for one or more of our product candidates, and even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.***

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan products by the EMA in the European Union. Generally, if a product candidate with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same product for the same therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our products, the agency must find that the product is indicated for the treatment of a condition or disease with a patient population of fewer than 200,000 individuals annually in the United States. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

***Our employees, principal investigators, consultants, and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.***

We are exposed to the risk of fraud or other misconduct by our employees, consultants, and commercial partners, and, if we commence clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the European Commission, and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing, and 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 restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, 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 government investigations or other actions or lawsuits stemming from a failure to comply with these laws or 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, financial condition, results of operations, and prospects, including the imposition of significant fines or other sanctions.

***Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates outside of the United States and require us to develop and implement costly compliance programs.***

We are subject to numerous laws and regulations in each jurisdiction outside the United States in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

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The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The Securities and Exchange Commission, or SEC, is involved with enforcement of the books and records provisions of the FCPA.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Our expansion outside of the United States has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain drugs and drug candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

### **Risks Related to Employee Matters and Managing Growth**

***Our future success depends on our ability to retain our Chief Executive Officer and other key executives and to attract, retain, and motivate qualified personnel.***

We are highly dependent on Katrine S. Bosley, our Chief Executive Officer, as well as the other principal members of our management and scientific teams. Ms. Bosley is employed “at will,” meaning we or she may terminate the employment relationship at any time. We do not maintain “key person” insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development, and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing, and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. 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. The inability to recruit, or loss of services of certain executives, key employees, consultants, or advisors, may impede the progress of our research, development, and commercialization objectives and have a material adverse effect on our business, financial condition, results of operations, and prospects.

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***We have expanded and expect to further expand our development, regulatory, and future sales and marketing capabilities, and as a result, we may encounter difficulties in 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 drug development, regulatory affairs, and sales and marketing. For example, our total number of employees grew from 55 to 89 from December 31, 2015 to December 31, 2016. 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 effectively manage the expected expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected physical 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 plans or disrupt our operations.

### **Risks Related to Our Common Stock**

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

Our shares of common stock began trading on The NASDAQ Global Select Market in February 2016. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares will not be sustained, which could put downward pressure on the market price of our common stock and thereby affect the ability of our stockholders to sell their shares.

***The market price of our common stock may be volatile, which could result in substantial losses for our stockholders.***

Our stock price has been, and is likely to remain, volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the success of existing or new competitive products or technologies;
- the timing and results of preclinical studies for our LCA10 program and any product candidates that we may develop;
- commencement or termination of collaborations for our product development and research programs;
- failure or discontinuation of any of our product development and research programs;
- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- developments or changing views regarding the use of genomic medicines, including those that involve genome editing;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs, or product candidates that we may develop;

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- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders, or other stockholders;
- expiration of market stand-off or lock-up agreements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions; and
- the other factors described in this “Risk Factors” section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. Following periods of such volatility in the market price of a company’s securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management’s attention and resources from our business.

***If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock and trading volume could decline.***

The trading market for our common stock depends, in part, on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock or fail to regularly publish reports on us, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

***A significant portion of our total outstanding shares may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.***

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock.

Moreover, holders of an aggregate of approximately 15.3 million shares of our common stock have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also have registered substantially all shares of common stock that we may issue under our equity compensation plans or that are issuable upon exercise of outstanding options. These shares can be freely sold in the public market upon issuance and once vested, subject to

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volume limitations applicable to affiliates. In addition, under the terms of certain of our license agreements and certain promissory notes that we have issued, and additional promissory notes that we may issue in the future in connection with these license agreements, we may elect to issue shares of our common stock in satisfaction of specified payment obligations of ours, which shares may be registered under the Securities Act or subject to rights requiring us to register such shares under the Securities Act. Such an election by us could result in the issuance of a substantial number of shares and upon registration under the Securities Act these shares would be able to be freely sold in the public market, subject to volume limitations applicable to affiliates. If any of the additional shares described above are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

In addition, certain of our employees, executive officers, directors, and affiliated stockholders have entered or may enter into Rule 10b5-1 plans providing for sales of shares of our common stock from time to time. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the employee, director or officer when entering into the plan, without further direction from the employee, officer, director, or affiliated stockholder. A Rule 10b5-1 plan may be amended or terminated in some circumstances. Our employees, executive officers, directors, and affiliated stockholders also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

***Our executive officers, directors, and principal stockholders, if they choose to act together, have the ability to control all matters submitted to stockholders for approval.***

As of January 1, 2017, our executive officers and directors, combined with our stockholders who owned more than 5% of our outstanding common stock, and their affiliates, in the aggregate, beneficially owned shares representing a majority of our outstanding common stock. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock.

***We are an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.***

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company until December 31, 2021. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or SOX Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the consolidated financial statements, reduced disclosure obligations regarding executive compensation, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders will be different than the information that is available with respect to other public companies. In particular, in this Annual Report on Form 10-K, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We expect to continue to take advantage of some of the reporting exemptions available to emerging growth companies. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, we are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

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

As a public company, and particularly after we are no longer an “emerging growth company,” we will incur significant legal, accounting, and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Select Market, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We have had to hire additional accounting, finance, and other personnel in connection with our becoming, and our efforts to comply with the requirements of being, a public company, and our management and other personnel devote a substantial amount of time towards maintaining compliance with these requirements. These requirements increase our legal and financial compliance costs and make some activities more time-consuming and costly. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to SOX Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by SOX Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements.

### ***We have broad discretion in the use of our cash reserves and may not use them effectively.***

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

### ***We do not expect to pay any dividends for the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investments.***

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

### ***Provisions in our restated certificate of incorporation and amended and restated bylaws or Delaware law might discourage, delay, or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.***

Provisions in our restated certificate of incorporation and amended and restated bylaws or Delaware law may discourage, delay, or prevent a merger, acquisition, or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock. These

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provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. These provisions include:

- limitations on the removal of directors;
- a classified board of directors so that not all members of our board of directors are elected at one time;
- advance notice requirements for stockholder proposals and nominations;
- the inability of stockholders to act by written consent or to call special meetings;
- the requirement that at least 75% of the votes cast by all our stockholders approve the amendment or repeal of certain provisions of our amended and restated bylaws or restated certificate of incorporation;
- the ability of our board of directors to make, alter, or repeal our amended and restated bylaws; and
- the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval, which could be used to institute a rights plan, or a poison pill, that would work to dilute the stock ownership of a potential hostile acquirer, likely preventing acquisitions that have not been approved by our board of directors.

In addition, Section 203 of the General Corporation Law of the State of Delaware prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

The existence of the foregoing provisions could deter potential acquirers of our company, thereby reducing the likelihood that our stockholders could receive a premium for their shares of common stock in an acquisition.

***Our restated certificate of incorporation designates the state courts in the State of Delaware or, if no state court located within the State of Delaware has jurisdiction, the federal court for the District of Delaware, as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors and officers.***

Our restated certificate of incorporation provides that, unless our board of directors otherwise determines, the state courts in the State of Delaware or, if no state court located within the State of Delaware has jurisdiction, the federal court for the District of Delaware, will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors or officers to our company or our stockholders, any action asserting a claim against us or any of our directors or officers arising pursuant to any provision of the General Corporation Law of the State of Delaware or our restated certificate of incorporation or amended and restated bylaws, or any action asserting a claim against us or any of our directors or officers governed by the internal affairs doctrine. This exclusive forum provision may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors or officers, which may discourage such lawsuits against us and our directors and officers.

### **Item 1B. Unresolved Staff Comments**

Not applicable.

### **Item 2. Properties.**

We lease approximately 59,783 square feet of office and laboratory space in Cambridge, Massachusetts under a lease that expires in November 2023, of which we occupy approximately 50,130 square feet and sublease approximately



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9,654 square feet under a sublease that expires in August 2018. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

### **Item 3. Legal Proceedings.**

From time to time, we may become involved in litigation or other legal proceedings relating to claims arising from the ordinary course of business. There can be no assurance that any proceedings that result from these third-party actions will be resolved in our favor. In addition, if they are not resolved in our favor, there can be no assurance that the result will not have a material adverse effect on our business, financial condition, results of operations, or prospects. For additional information regarding these matters set forth in this section, see “Risk Factors—Risks Related to Our Intellectual Property—Some of our in-licensed patents are subject to priority disputes” and “Business—Intellectual Property.” Regardless of outcome, litigation or other legal proceedings can have an adverse impact on us because of defense and settlement costs, diversion of management resources, and other factors.

On January 11, 2016 and March 17, 2016, the Patent Trial and Appeal Board, or PTAB, of the United States Patent and Trademark Office, or USPTO, declared an interference between a pending U.S. patent application (U.S. Serial No. 13/842,859) that is owned by the University of California, the University of Vienna, and Emmanuelle Charpentier and 12 U.S. patents (U.S. Patent Nos. 8,697,359; 8,771,945; 8,795,965; 8,865,406; 8,871,445; 8,889,356; 8,895,308; 8,906,616; 8,932,814; 8,945,839; 8,993,233; and 8,999,641) and a pending U.S. patent application (U.S. Serial No. 14/704,551) that are co-owned by Broad, MIT, and in some cases Harvard, and in-licensed by us. An interference is a proceeding within the USPTO to determine priority of invention of the subject matter of patent claims filed by different parties. In the declared interference, the University of California, acting on behalf of itself and the University of Vienna, and Emmanuelle Charpentier were designated as the senior party and Broad was designated as the junior party.

On February 15, 2017, the PTAB held that there is no interference-in-fact, which means that no interference is needed to resolve priority between the parties because the PTAB determined that the Broad claims are directed to subject matter that is patentably distinct from those of the University of California, the University of Vienna, and Emmanuelle Charpentier. The interference proceeding has therefore ended. Therefore, the 12 U.S. patents and one U.S. patent application that we have in-licensed from Broad, acting on behalf of itself, MIT, and Harvard, as well as the U.S. patent application owned by the University of California, the University of Vienna, and Emmanuelle Charpentier, with respect to which the PTAB had declared an interference were not modified or revoked as a result of this interference proceeding. However, the University of California, the University of Vienna, and Emmanuelle Charpentier may request a rehearing of the judgment by the PTAB within 30 days and/or may appeal to the Court of Appeals for the Federal Circuit within 63 days.

Separately, ToolGen Inc., or ToolGen, also filed Suggestions of Interference in the USPTO on April 13, 2015, which became publicly available on November 12, 2015 and December 3, 2015, against five U.S. patents, which are among the 12 U.S. patents with respect to which the PTAB had declared an interference and which we have in-licensed from Broad, acting on behalf of itself, MIT, and Harvard. The Suggestions of Interference that were filed by ToolGen are still pending and it is uncertain when and in what manner the USPTO will act on them.

On May 9, 2016, the USPTO granted a request for *ex parte* re-examination of U.S. Patent No. 8,771,945, which is among the 12 U.S. patents with respect to which the PTAB had declared an interference and which we have in-licensed from Broad, acting on behalf of itself and MIT. On May 12, 2016, the PTAB suspended the re-examination of U.S. Patent No. 8,771,945 noting that it has jurisdiction over any file that involves a patent involved in the interference. It is uncertain when the PTAB will lift the suspension, however the PTAB may do so in light of the PTAB’s no interference-in-fact holding.

The European Patent Office Opposition Division has initiated opposition proceedings in the European Patent Office against four European patents that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard and one European patent that we have in-licensed from Broad, acting on behalf of itself and MIT. Oppositions have also been filed against two other European patents that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard.

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**Item 4. Mine Safety Disclosures.**

Not applicable.

**PART II****Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.****Market Information**

Our common stock trades on the NASDAQ Global Select Market under the symbol “EDIT”. Trading of our common stock commenced on February 3, 2016 in connection with our initial public offering, or IPO. Prior to that time, there was no established public trading market for our common stock. The following table sets forth for the period indicated the high and low sale prices per share for our common stock as reported on the NASDAQ Global Select Market for the period indicated:

2016	Market Price	
	High	Low
First Quarter (beginning February 3, 2016)	\$ 43.99	\$ 12.57
Second Quarter	\$ 43.50	\$ 22.50
Third Quarter	\$ 28.63	\$ 13.10
Fourth Quarter	\$ 18.94	\$ 12.43

**Holders**

As of January 1, 2017, we had approximately 38 holders of record of our common stock. This number does not include beneficial owners whose shares were held in street name.

**Dividend Policy**

We have never declared or paid any cash dividends on our common stock. We currently intend to retain future earnings to fund the development and growth of our business. We do not expect to pay any cash dividends in the foreseeable future. In addition, the terms of any future debt agreements that we may enter into, may preclude us from paying dividends without the lenders’ consent or at all.

**Securities Authorized for Issuance under Equity Compensation Plans**

Information about our equity compensation plans is incorporated herein by reference to the section entitled “Securities authorized for issuance under equity compensation plans” in Item 12 of Part III of this Annual Report on Form 10-K.

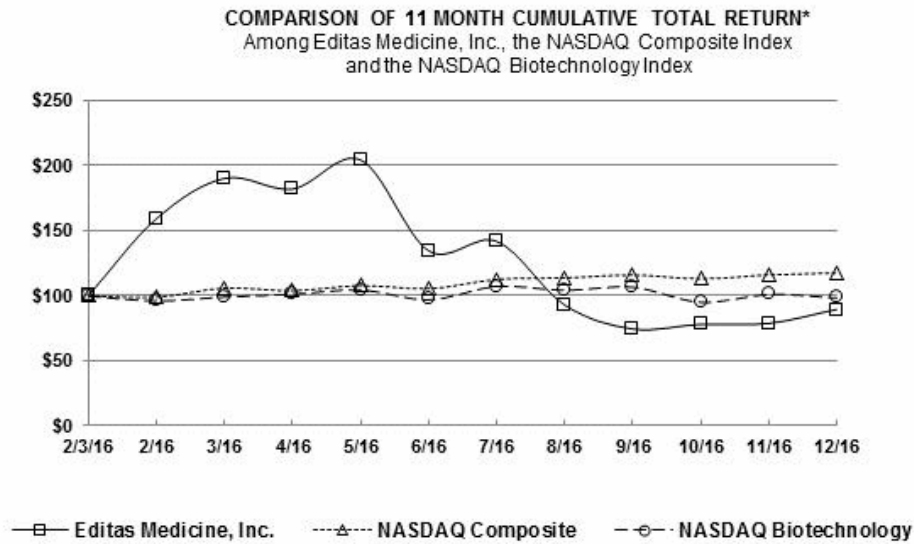
**Performance Graph**

The following performance graph and related information shall not be deemed to be “soliciting material” or to be “filed” with the SEC for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liabilities under that Section, nor shall such information be incorporated by reference into any future filing under the Exchange Act or the Securities Act of 1933, as amended, or the Securities Act, except to the extent that we specifically incorporate it by reference into such filing.

The following graph compares the performance of our common stock to The NASDAQ Composite Index and to The NASDAQ Biotechnology Index from February 3, 2016 (the first date on which shares of our common stock were publicly traded) through December 31, 2016. The comparison assumes \$100 was invested after the market closed on

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February 3, 2016 in our common stock and in each of the foregoing indices, and it assumes reinvestment of dividends, if any. The stock price performance included in this graph is not necessarily indicative of future stock price performance.



\* \$100 invested on 2/3/16 in stock or in index, including reinvestment of dividends

**Recent Sales of Unregistered Securities**

In December 2016, in connection with our entry into certain license agreements with the Broad Institute, Inc., or the Broad, we issued promissory notes, or the Notes, in an aggregate principal amount of \$10.0 million to Broad and Wageningen University. The Notes are convertible, at our option, into shares of our common stock subject to certain conditions. No underwriters were involved in the foregoing issuances of securities. The securities were issued pursuant to Section 4(a)(2) under the Securities Act, relating to transactions by an issuer not involving any public offering. All recipients either received adequate information about us or had access, through other relationships, to such information.

**Purchase of Equity Securities**

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

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**Use of Proceeds from Registered Securities**

On February 8, 2016, we closed our initial public offering of common stock under a registration statement on Form S-1 (File No. 333-208856) that was declared effective by the Securities and Exchange Commission, or the SEC, on February 2, 2016.

We received aggregate net proceeds from the offering of \$97.5 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. None of the underwriting discounts and commissions or other offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10% or more of our common stock or to any affiliates of ours.

As of December 31, 2016, we had used approximately \$24.6 million of the net offering proceeds, primarily to fund preclinical studies for our LCA10 program, continued expansion of our platform technology, and preclinical studies of our research programs in addition to LCA10 and engineered T cells, as well as for working capital and general corporate purposes. We have invested the remaining net proceeds from the offering in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities. There has been no material change in our planned use of the net proceeds from the offering as described in the final prospectus for our initial public offering filed with the SEC pursuant to Rule 424(b) under the Securities Act.

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**Item 6. Selected Consolidated Financial Data.**

You should read the following selected consolidated financial data together with our consolidated financial statements and accompanying notes appearing elsewhere in this Annual Report on Form 10-K and the “Management’s Discussion and Analysis of Financial Condition and Results of Operations” section of this Annual Report on Form 10-K. We have derived the consolidated statement of operations data for the years ended December 31, 2016, 2015 and 2014 and the consolidated balance sheet data as of December 31, 2016 and 2015 from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. We have derived the consolidated statements of operations data from the period ended December 31, 2013 and consolidated balance sheet data as of December 31, 2014 and 2013 from our audited consolidated financial statements not included in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of the results that may be expected in any future period.

	2016	Year Ended December 31, 2015	2014	Period from September 3, 2013 (Inception) to December 31, 2013
(in thousands, except share and per share data)				
<b>Consolidated Statements of Operations Data:</b>				
Collaboration and other research and development revenues	\$ 6,053	\$ 1,629	\$ —	\$ —
Operating expenses:				
Research and development	56,979	18,846	5,073	530
General and administrative	46,262	18,095	7,650	1,210
Total operating expenses	103,241	36,941	12,723	1,740
Operating loss	(97,188)	(35,312)	(12,723)	(1,740)
Other expense, net	(57)	(37,445)	(928)	(18)
Interest income (expense), net	62	(143)	(34)	—
Total other income (expense), net	5	(37,588)	(962)	(18)
Net loss and comprehensive loss	\$ (97,183)	\$ (72,900)	\$ (13,685)	\$ (1,758)
Reconciliation of net loss to net loss attributable to common stockholders:				
Net loss	\$ (97,183)	\$ (72,900)	\$ (13,685)	\$ (1,758)
Accretion of redeemable convertible preferred stock to redemption value <sup>(1)</sup>	(47)	(394)	(309)	(25)
Net loss attributable to common stockholders <sup>(1)</sup>	\$ (97,230)	\$ (73,294)	\$ (13,994)	\$ (1,783)
Net loss per share attributable to common stockholders, basic and diluted <sup>(1)</sup>	\$ (3.02)	\$ (28.55)	\$ (12.46)	\$ (5.93)
Weighted-average common shares outstanding, basic and diluted <sup>(1)</sup>	32,219,717	2,566,916	1,123,098	300,480

- (1) See Note 14 to our consolidated financial statements for further details on the calculation of net loss per share, basic and diluted, attributable to common stockholders and the weighted-average number of shares used in the computation of the per share amounts.

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	<u>2016</u>	<u>December 31,</u>		<u>2013</u>
		<u>2015</u>	<u>2014</u>	
(in thousands)				
<b>Consolidated Balance Sheet Data:</b>				
Cash and cash equivalents	\$ 185,323	\$ 143,180	\$ 10,623	\$ 2,012
Working capital	154,100	138,060	4,555	(39)
Total assets	229,182	149,363	12,188	2,481
Deferred revenue, net of current portion	26,000	25,321	—	—
Construction financing lease obligation, net of current portion	35,096	—	—	—
Equipment loan, net of current portion and discounts	—	—	344	—
Redeemable convertible preferred stock	—	199,915	20,772	2,111
Total stockholders' equity (deficit)	134,607	(83,114)	(15,292)	(1,763)



**Item 7. 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 appearing elsewhere in this Annual Report on Form 10-K.*

*Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. There are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by forward-looking statements. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the section entitled “Risk Factors” in Part II, Item 1A that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make.*

*You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.*

**Overview**

We are a leading genome editing company dedicated to treating patients with genetically defined diseases by correcting their disease-causing genes. Our mission is to translate the promise of genome editing science into a broad class of transformative genomic medicines to benefit the greatest number of patients. To this end, we are developing a proprietary genome editing platform based on CRISPR technology. Our product development strategy is to target genetically defined diseases with an initial focus on debilitating illnesses where there are no approved treatments and where the genetic basis of disease is well understood. Over time, we also intend to develop medicines that may address genetically treatable diseases in addition to genetically defined diseases. A genetically defined disease may be treated by correcting a disease-causing gene, whereas a genetically treatable disease is a disease that does not necessarily have a single, disease-causing gene, but which nonetheless may be treated by editing genes to ameliorate or eliminate the signs or symptoms of that disease. We are advancing discovery research programs, including programs to address genetic, infectious, and oncologic diseases of the liver, lung, blood, eye, and muscle. Our most advanced program is designed to address a specific genetic form of retinal degeneration called Leber Congenital Amaurosis type 10, or LCA10, a disease for which we are not aware of any available therapies or potential treatments in clinical trials in either the United States or European Union. We aim to initiate a clinical natural history study in mid-2017 to evaluate the clinical course and characteristics of LCA10 more extensively, and we aim to file an investigational new drug, or IND, application by the end of 2017 for our LCA10 program. In May 2015, we entered into a collaboration with Juno Therapeutics, Inc., or Juno Therapeutics, a leader in the emerging field of immuno-oncology, to develop novel engineered T cell therapies for cancer.

Since our inception in September 2013, our operations have focused on organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio, assembling our core capabilities in genome editing, seeking to identify potential product candidates, and undertaking preclinical studies. All of our research programs are still in the preclinical or research stage of development and their risk of failure is high. We have not generated any revenue from product sales. We have funded our operations primarily through the initial public offering of our common stock, or IPO, private placements of our preferred stock, an equipment loan, and payments received under our collaboration with Juno Therapeutics and our award agreement with the Cystic Fibrosis Foundation

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Therapeutics, Inc., or CFFT. From inception through December 31, 2016, we raised an aggregate of \$295.4 million to fund our operations.

In February 2016, we completed our IPO and sold 6,785,000 shares of our common stock, including 885,000 shares of our common stock pursuant to the full exercise by the underwriters of an option to purchase additional shares, at a public offering price of \$16.00 per share for an aggregate offering of approximately \$108.6 million. We received aggregate net proceeds from the IPO of approximately \$97.5 million, after deducting underwriting discounts and commissions and other offering expenses payable by us.

Since inception, we have incurred significant operating losses. Our net losses were \$97.2 million, \$72.9 million, and \$13.7 million for the years ended December 31, 2016, 2015, and 2014, respectively. As of December 31, 2016, we had an accumulated deficit of \$185.5 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and from year to year. We anticipate that our expenses will increase substantially as we continue our current research programs and our preclinical development activities; seek to identify additional research programs and additional product candidates; initiate preclinical testing and clinical trials for any product candidates we identify and develop; maintain, expand, and protect our intellectual property portfolio, including reimbursing our licensors for such expenses related to the intellectual property that we in-license from such licensors; further develop our genome editing platform; hire additional clinical, quality control, and scientific personnel; and incur additional costs associated with operating as a public company. We do not expect to be profitable for the year ending December 31, 2017 or the foreseeable future.

### **Financial Operations Overview**

#### ***Revenue***

To date, we have not generated any revenue from product sales and we do not expect to generate any revenue from product sales for the foreseeable future. In connection with entering into our collaboration with Juno Therapeutics in May 2015, we received an upfront payment of \$25.0 million, and in May 2016, we received a milestone payment of \$2.5 million. In addition, we will receive up to \$22.0 million in research support over the five years of the collaboration and across the three programs under the collaboration, subject to adjustment in accordance with the terms of the agreement. Through December 31, 2016, we had recognized an aggregate of \$4.8 million of research support from Juno Therapeutics since entering into the agreement, including \$3.2 million that was recognized during the year ended December 31, 2016.

For the year ended December 31, 2016, we recognized \$5.7 million of collaboration revenue related to our collaboration with Juno Therapeutics, including \$2.5 million recognized during the second quarter in connection with the achievement of our first milestone under the collaboration, resulting from technical progress in a research program under the collaboration. For additional information about our revenue recognition policy related to the Juno Therapeutics collaboration, see “—Critical Accounting Policies and Estimates—Revenue.”

In May 2016, we entered into an award agreement with CFFT, pursuant to which CFFT has agreed to pay us up to \$5.0 million over the agreement’s three year term to support our cystic fibrosis development program and related technology research and development. Under the terms of the agreement, we are required to contribute additional funds to the program in an amount equal to the funds contributed by CFFT and to pay certain amounts to CFFT upon the achievement of specified events. For the year ended December 31, 2016, we recognized \$0.3 million of revenue related to our agreement with CFFT.

For the foreseeable future, we expect substantially all of our revenue will be generated from our collaboration with Juno Therapeutics, our agreement with CFFT, any other collaborations or agreements we may enter into, and rental payments from our subtenant.

**Expenses**

*Research and Development Expenses*

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts and preclinical studies under our research programs, which include:

- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- costs of funding research performed by third parties that conduct research and development and preclinical activities on our behalf;
- costs of purchasing lab supplies and non-capital equipment used in our preclinical activities and in manufacturing preclinical study materials;
- consultant fees;
- facility costs including rent, depreciation, and maintenance expenses; and
- fees for acquiring and maintaining licenses under our third-party licensing agreements.

Research and development costs are expensed as incurred. At this time, we cannot reasonably estimate or know the nature, timing, and estimated costs of the efforts that will be necessary to complete the development of any product candidates we may identify and develop. This is due to the numerous risks and uncertainties associated with developing such product candidates, including the uncertainty of:

- successful completion of preclinical studies and Investigational New Drug-enabling studies;
- successful enrollment in, and completion of, clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity;
- launching commercial sales of the product, if and when approved, whether alone or in collaboration with others;
- acceptance of the product, if and when approved, by patients, the medical community, and third-party payors;
- effectively competing with other therapies and treatment options;
- a continued acceptable safety profile following approval;
- enforcing and defending intellectual property and proprietary rights and claims; and
- achieving desirable medicinal properties for the intended indications.

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A change in the outcome of any of these variables with respect to the development of any product candidates we may develop would significantly change the costs, timing, and viability associated with the development of that product candidate.

Other than in connection with our collaboration with Juno Therapeutics and our agreement with CFFT, we do not track research and development costs on a program-by-program basis as we have not yet identified a product candidate for advancement into clinical trials. We plan to track research and development costs for any individual development program when we identify a product candidate from the program that we believe we can advance into clinical trials.

Research and development activities are central to our business model. We expect research and development costs to increase significantly for the foreseeable future as our development programs progress, including as we continue to support the preclinical studies for our LCA10 program as well as our other research programs.

### *General and Administrative Expenses*

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation for personnel in executive, finance, investor relations, business development, legal, corporate affairs, and human resource functions. Other significant costs include corporate facility costs not otherwise included in research and development expenses, legal fees related to patent and corporate matters, and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future to support continued research and development activities and potential commercialization of any product candidates we identify and develop. These increases will include increased costs associated with the lease of a new facility for our headquarters and will likely include increased costs related to the hiring of additional personnel, and fees to outside consultants. We also anticipate increased expenses related to reimbursement of third-party patent-related expenses and increased expenses associated with being a public company, including costs for audit, legal, regulatory, and tax-related services, director and officer insurance premiums, and investor relations costs. With respect to reimbursement of third-party patent-related expenses specifically, given the ongoing nature of the interference and opposition proceedings involving the patents licensed to us under our license agreement with The Broad Institute, Inc., or Broad, and the President and Fellows of Harvard College, or Harvard, as described in more detail in “Risk Factors—Risks Related to Our Intellectual Property.” Some of our in-licensed patents are subject to priority disputes, we anticipate that our obligation to reimburse Broad and Harvard for expenses related to these proceedings during future periods will be substantial until such interference and opposition proceedings are resolved.

### *Other Income (Expense), Net*

Other income (expense), net consists primarily of interest income earned on our cash equivalents and government grant income, net of re-measurement losses associated with changes in the fair value of our liability for a warrant to purchase preferred stock. Upon the completion of our IPO, all of our preferred stock converted into common stock on a 2.6-for-one basis and our outstanding warrant to purchase preferred stock converted into a warrant to purchase common stock and we reclassified the fair value of the warrant to additional paid-in capital. As a result, we ceased recognizing further re-measurement gains or losses associated with the warrant after the first quarter of 2016.

Prior to 2016, other income (expense), net included re-measurement gains or losses associated with changes in the fair value of the tranche rights associated with our Series A-1 preferred stock and anti-dilutive protection liability associated with our issuance of common stock to certain licensors. In June 2015, upon the issuance of the final tranche of our Series A preferred stock, the tranche right liability was settled and reclassified to Series A preferred stock and the anti-dilutive protection liability was settled and reclassified to additional paid-in-capital. Therefore no further re-measurement gains or losses will be recognized related to the tranche rights or the anti-dilutive protection liability.

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**Critical Accounting Policies and Estimates**

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of our consolidated financial statements requires us to make judgments and estimates that affect the reported amounts of assets, liabilities, revenues, and expenses, and the disclosure of contingent liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events, and various other factors that we believe to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts, and experience. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies used in the preparation of our consolidated financial statements require the most significant judgments and estimates.

***Revenue Recognition***

As of December 31, 2016, all of our revenue to date had been generated from our collaboration with Juno Therapeutics and our award agreement with CFFT. We recognize revenue in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605, *Revenue Recognition*, or ASC 605. Accordingly, revenue is recognized 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.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in our consolidated balance sheets.

***Multiple Element Arrangements***

***Determination of Accounting Units***

We analyze multiple element arrangements based on the guidance in ASC Topic 605-25, *Revenue Recognition—Multiple Element Arrangements*, or ASC 605-25. Pursuant to the guidance in ASC 605-25, we evaluate multiple element arrangements to determine (1) the deliverables included in the arrangement and (2) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separate from other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: (i) the delivered item(s) has value to the customer on a standalone basis and (ii) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially within our control. In assessing whether an item under a collaboration has standalone value, we consider factors such as the research, manufacturing, and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. We also consider whether our collaboration partner can use the other deliverable(s) for their intended purpose without the receipt of the remaining element(s), whether the value of the deliverable is dependent on the undelivered item(s), and whether there are other vendors that can provide the undelivered element(s).

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Options under a collaboration are considered substantive if, at the inception of the arrangement, we are at risk as to whether the collaboration partner will choose to exercise the option. Factors that we consider in evaluating whether an option is substantive include the cost to exercise the option, the overall objective of the arrangement, the benefit the collaboration partner might obtain from the arrangement without exercising the option, and the likelihood the option will be exercised. When an option is considered substantive, we would not consider the option or item underlying the option to be a deliverable at the inception of the arrangement and the associated option fees are not included in allocable consideration, assuming the option is not priced at a significant and incremental discount. Conversely, when an option is not considered substantive, we would consider the option, including other deliverables contingent upon the exercise of the option, to be a deliverable at the inception of the arrangement and a corresponding amount would be included in allocable arrangement consideration. In addition, if the price of the option includes a significant incremental discount, the discount would be included as a deliverable at the inception of the arrangement.

### Allocation of Arrangement Consideration

Arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method. The applicable revenue recognition criteria in ASC 605 are applied to each of the separate units of accounting in determining the appropriate period and pattern of recognition. We determine the selling price of a unit of accounting following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, we determine the estimated selling price for units of accounting within each arrangement using vendor specific objective evidence, or VSOE, of selling price, if available, third-party evidence, or TPE, of selling price if VSOE is not available, or best estimate of selling price, or BESP, if neither VSOE or TPE is available. We have only used BESP to estimate selling price, since we have not had VSOE or TPE of selling price for any units of accounting to date. Determining BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the applicable agreement and estimated costs. We validate BESP for units of accounting by evaluating whether changes in the key assumptions used by us to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

### Pattern of Recognition

We recognize the arrangement's consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605 are satisfied for that particular unit of accounting. We will recognize revenue associated with licenses, license options, or the discount related to a license option upon (i) delivery of the license or (ii) the earlier of exercise or expiration of the license option, if the underlying license has standalone value from the other deliverables to be provided after delivering that license. If the license does not have standalone value, the amounts allocated to the license will be combined with the related undelivered items as a single unit of accounting.

We recognize the amounts associated with collaboration research and development services, joint research committees, or other services ratably over the associated period of performance. 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 that we are expected to complete our performance obligations. Conversely, if the pattern of performance in which the service is provided to the collaboration partner can be determined and objectively measurable performance exists, 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 revenue earned determined using the straight line method or proportional performance, as applicable, as of the period end date.

### Recognition of Milestones and Royalties

At the inception of an arrangement that includes milestone payments, 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: (1) the consideration is commensurate with either our performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from our performance to achieve the milestone, (2) the consideration relates solely to past performance, and (3) the consideration is reasonably

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relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as clinical, regulatory, commercial, and other risks that must be overcome to achieve the respective milestones and the level of effort and investment required to achieve the respective milestones 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. In accordance with ASC Topic 605-28, *Revenue Recognition—Milestone Method*, or ASC 605-28, a clinical or regulatory milestone that is considered substantive will be recognized as revenue in its entirety upon successful accomplishment of the milestone, assuming all other revenue recognition criteria are met. Milestones that are not considered substantive would be recognized as revenue over the remaining period of performance, assuming all other revenue recognition criteria are met. Revenue from a commercial milestone payment will be accounted for as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

We will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable, we have no remaining performance obligations, and assuming all other revenue recognition criteria are met.

### ***Accrued Research and Development Expenses***

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

We record our expenses related to research and development activities based on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.



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***Construction Financing Lease Obligation***

Beginning in 2016, we began recording certain estimated construction costs incurred and reported to us by a landlord as an asset and corresponding construction financing lease obligation on our consolidated balance sheets because we were deemed to be the owner of the building during the construction period for accounting purposes. In each reporting period, the landlord estimated and reported to us the costs incurred to date and provided supporting invoices for management to review. We periodically met with the landlord and its construction manager to review the estimates and observe construction progress prior to recording such amounts. Construction was completed in October 2016 and we considered the requirements for sale-leaseback accounting treatment, which included an evaluation of whether all risks of ownership had transferred back to the landlord as evidenced by a lack of continuing involvement in the lease property. We determined that the arrangement did not qualify for sale lease-back accounting treatment, the building asset will remain on our balance sheet at its historical cost, and such asset would be depreciated over its estimated useful life of thirty years.

***Fair Value Measurements***

*Warrants*

In conjunction with an equipment loan financing in 2014, we issued to Silicon Valley Bank a warrant to purchase up to 60,000 shares of our Series A-1 preferred stock at an exercise price of \$1.00 per share. The fair value of the warrant at the issuance date was recorded as a reduction to face value of the debt balance and was amortized as interest expense, along with other debt issuance costs, over the term of the loan. Due to the liquidation preferences of the Series A-1 preferred stock, we recorded the warrant as a liability on our consolidated balance sheets. Following a reverse stock split in January 2016 and the closing of our IPO in February 2016, such warrant converted into a warrant to purchase 23,076 shares of our common stock, which Silicon Valley Bank fully exercised in February 2016 pursuant to a net exercise provision for an aggregate of 19,271 shares of our common stock.

*Tranche Rights*

The Series A preferred stock purchase agreement that we entered into provided the investors with the right, upon achievement of certain milestones, to participate in subsequent offerings of Series A preferred stock, which we refer to as tranche rights. The tranche rights met the definition of a freestanding financial instrument, as the tranche rights were legally detachable and separately exercisable from the Series A preferred stock. Since the Series A preferred stock was redeemable at the holder's option subject to certain limitations, the tranche rights were classified as an asset or liability and were initially recorded at fair value and then marked to market at each subsequent reporting period, through the settlement of the tranche rights.

We determined fair value utilizing the concept of "Fair Value" from ASC Topic 820, *Fair Value Measurement*, or ASC 820, which states that any fair value measurement requires that the reporting entity to determine the valuation technique(s) appropriate for the measurement, considering the availability of data with which to develop inputs that represent the assumptions that market participants would use in pricing the asset or liability and the level in the fair value hierarchy within which the inputs are categorized.

The estimated fair value of the tranche rights was determined using a probability-weighted present value model that considered the probability and timing of closing a tranche, the estimated future value of the Series A preferred stock to be issued at each closing, and the amount of the investment required at each closing. Future values were converted to present value using a discount rate appropriate for probability-adjusted cash flows. Upon the settlement of each tranche, the fair value of the tranche rights associated with that tranche was reclassified to Series A preferred stock at its then fair value and thereafter was no longer re-measured.

***Stock-based Compensation***

We account for our stock-based compensation awards in accordance with ASC Topic 718, *Compensation—Stock Compensation*, or ASC 718. ASC 718 requires all share-based payments to employees, including grants of

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employee stock options, to be recognized as expense in the consolidated statements of operations based on their grant date fair values. For stock options granted to employees and to members of our board of directors for their services on our board of directors, we estimate the grant date fair value of each option award using the Black-Scholes option-pricing model. For stock options subject to service-based vesting conditions, we recognize stock-based compensation expense equal to the grant date fair value of stock options on a straight-line basis over the requisite service period.

Share-based payments issued to non-employees are initially recorded at their fair values, and are revalued at each reporting date and as the equity instruments vest and are recognized as expense over the related service period in accordance with the provisions of ASC Topic 505-50, *Equity-Based Payments to Non-Employees*.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (1) the expected stock price volatility, (2) the calculation of expected term of the award, (3) the risk-free interest rate, and (4) the expected dividend yield. Because there had been no public market for our common stock prior to our IPO, there is a lack of company-specific historical and implied volatility data. Accordingly, we base our estimates of expected volatility on the historical volatility of a group of similar companies that are publicly traded. We calculate historical volatility based on a period of time commensurate with the expected term. We compute expected volatility based on the historical volatility of a representative group of companies with similar characteristics to us, including their stages of product development and focus on the life science industry. We use the simplified method as prescribed by the Securities and Exchange Commission's Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term for options granted to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. For options granted to non-employees, we utilize the contractual term of the arrangement as the basis for the expected term. We determine the risk-free interest rate based on a treasury instrument whose term is consistent with the expected term of the stock options. We use an assumed dividend yield of zero as we have never paid dividends and do not have current plans to pay any dividends on common stock. If factors change or different assumptions are used, our stock-based compensation expense could be materially different in the future.

The weighted-average assumptions used in the Black-Scholes option pricing model to determine the fair value of stock options granted to employees and directors were as follows:

	Year Ended December 31,		
	2016	2015	2014
Expected volatility	78.4 %	78.8 %	87.6 %
Expected term (in years)	6.25	6.25	6.25
Risk-free interest rate	1.5 %	1.7 %	1.9 %
Expected dividend yield	—	—	—

The weighted average assumptions used in the Black-Scholes option pricing model to determine the fair value of stock options granted to non-employees other than directors were as follows:

	Year Ended December 31,		
	2016	2015	2014
Expected volatility	76.5 %	80.0 %	80.5 %
Expected term (in years)	10.0	10.0	9.5
Risk-free interest rate	1.6 %	2.2 %	1.5 %
Expected dividend yield	—	—	—

Stock-based compensation totaled approximately \$16.9 million, \$3.5 million, and \$0.1 million for the years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016, we had \$3.4 million and \$24.5 million of unrecognized compensation expense related to restricted stock awards and stock option awards, respectively, which are expected to be recognized over weighted-average remaining vesting periods of approximately 0.6 and 3.0 years, respectively. We expect the impact of our stock-based compensation expense for restricted stock and stock

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options granted to employees and non-employees to grow in future periods due to the potential increases in the value of our common stock and headcount.

### *Determination of Fair Value of Common Stock on Grant Dates prior to our Initial Public Offering*

We historically have granted stock options and restricted stock at exercise or purchase prices not less than the fair value of our common stock. Due to the absence of an active market for our common stock prior to our IPO, the estimated fair values of our common stock as of grant dates prior to our IPO were determined contemporaneously by our board of directors. From 2014 through the date of our IPO, our board of directors' determinations involved the preparation of valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, also known as the Practice Aid. Following our IPO, it is no longer necessary for us to estimate the fair value of our common stock in connection with our accounting for stock options or other equity awards, as the fair value of our common stock can be determined by reference to its closing price on The NASDAQ Global Select Market on the date of the applicable grant.

Our board of directors performed contemporaneous common stock valuations as of August 4, 2015 and October 23, 2015 and retrospective common stock valuations as of April 16, 2015, June 1, 2015, and September 14, 2015. In conducting these valuation analyses, our board of directors considered all objective and subjective factors that it believed to be relevant for each valuation conducted, including the lack of an active public market for our common and our convertible preferred stock; the prices of shares of our convertible preferred stock that we had sold to outside investors in arm's length transactions, and the rights, preferences, and privileges of that convertible preferred stock relative to our common stock; our results of operations and financial condition; our entry into license agreements, pursuant to which we obtained rights to important intellectual property; the material risks related to our business; our business strategy; the market performance of publicly traded companies in the life sciences and biotechnology sectors; and the likelihood of achieving a liquidity event for the holders of our common stock, such as an IPO, given prevailing market conditions.

### *Stock Option Grants in Connection with and Following Initial Public Offering*

Our board of directors approved, effective upon the commencement of trading of our common stock on The NASDAQ Global Select Market, grants of stock options to purchase an aggregate of 496,727 shares of common stock at a purchase price per share equal to the estimated fair market value of our common stock on such date of grant, which our board of directors determined to be equal to the initial public offering price of our common stock.

Since our IPO, the exercise price per share of all option grants has been set at the closing price of our common stock on The NASDAQ Global Select Market on the applicable date of grant, which our board of directors believes represents the fair value of our common stock.

[Table of Contents](#)**Results of Operations****Comparison of Years ended December 31, 2016 and 2015**

The following table summarizes our results of operations for the years ended December 31, 2016 and 2015, together with the changes in those items in dollars (in thousands):

	<b>Year Ended December 31,</b>		<b>Dollar Change</b>
	<b>2016</b>	<b>2015</b>	
Collaboration and other research and development revenues	\$ 6,053	\$ 1,629	\$ 4,424
Operating expenses:			
Research and development	56,979	18,846	38,133
General and administrative	46,262	18,095	28,167
Total operating expenses	<u>103,241</u>	<u>36,941</u>	<u>66,300</u>
Other income (expense), net:			
Other expense, net	(57)	(37,445)	37,388
Interest income (expense), net	62	(143)	205
Total other income (expense), net	<u>5</u>	<u>(37,588)</u>	<u>37,593</u>
Net loss	<u>\$ (97,183)</u>	<u>\$ (72,900)</u>	<u>\$ (24,283)</u>

*Collaboration and Other Research and Development Revenues*

Collaboration and other research and development revenues were \$6.1 million for the year ended December 31, 2016 and consisted of \$5.7 million of revenue recognized pursuant to our collaboration with Juno Therapeutics, including \$2.5 million recognized in connection with a milestone payment, and \$0.3 million of revenue recognized pursuant to our agreement with CFFT. Collaboration and other research and development revenues were \$1.6 million for the year ended December 31, 2015 and consisted of revenue recognized pursuant to our collaboration with Juno Therapeutics.

*Research and Development Expenses*

Research and development expenses increased by \$38.1 million, to \$57.0 million for the year ended December 31, 2016 from \$18.8 million for the year ended December 31, 2015. The following table summarizes our research and development expenses for the years ended December 31, 2016 and December 31, 2015, together with the changes in those items in dollars (in thousands):

	<b>Year Ended December 31,</b>		<b>Dollar Change</b>
	<b>2016</b>	<b>2015</b>	
Employee and non-employee related expenses	\$ 22,819	\$ 8,203	\$ 14,616
Process and platform development expenses	10,333	3,957	6,376
License fees and expenses	17,715	4,603	13,112
Facility expenses	5,671	1,805	3,866
Other expenses	441	278	163
Total research and development expenses	<u>\$ 56,979</u>	<u>\$ 18,846</u>	<u>\$ 38,133</u>

The increase in research and development expenses for the year ended December 31, 2016 compared to the year ended December 31, 2015 was primarily attributable to:

- approximately \$14.6 million in increased research and development employee and non-employee compensation costs, including stock-based compensation, resulting from an increase in the size of our workforce and the hiring of key executives throughout 2016, with the non-employee costs relating to contractors and founders;
- approximately \$13.1 million in increased license fees related to our license agreements that were executed in 2016 with The General Hospital Corporation, d/b/a Massachusetts General Hospital, or MGH, and

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Broad, partially offset by a decrease from fees paid to licensors during the second quarter of 2015 as a result of our entry into our collaboration agreement with Juno Therapeutics that did not recur in 2016;

- approximately \$6.4 million in increased process and platform development costs due to increased research activity;
- approximately \$3.9 million in increased facilities costs, including rent, utilities, and depreciation expense as a result of additional office and laboratory space; and
- approximately \$0.1 million in increased other expenses.

### *General and Administrative Expenses*

General and administrative expenses increased by \$28.2 million, to \$46.3 million for the year ended December 31, 2016 from \$18.1 million for the year ended December 31, 2015. The increase in general and administrative expenses was primarily attributable to:

- approximately \$16.5 million in increased legal and patent-related fees, including expenses associated with the prosecution and maintenance of the patents and patent applications owned by us or licensed to us;
- approximately \$7.2 million in increased employee compensation cost;
- approximately \$2.4 million in increased contractor consulting fees; and
- approximately \$2.1 million in increased other general and administrative expenses including office and facility related costs resulting from our move to our new corporate headquarters during the fourth quarter of 2016.

### *Other Income (Expense), Net*

Other income (expense), net was \$5 thousand for the year ended December 31, 2016 and \$37.6 million for the year ended December 31, 2015. The decrease was primarily related to \$35.6 million in expense in 2015 related to mark-to-market adjustments in our Series A preferred stock tranche right liability. The tranche right liability was settled in June 2015.

The decrease in other income (expense), net was also attributable in part to a \$1.6 million mark-to-market adjustment recorded in June 2015 for the anti-dilution protection liability related to our issuance of common stock to our licensors. The anti-dilution liability was settled in June 2015.

[Table of Contents](#)**Comparison of Years Ended December 31, 2015 and 2014**

The following table summarizes our results of operations for the years ended December 31, 2015 and 2014, together with the changes in those items in dollars (in thousands):

	Year Ended December 31,		Dollar Change
	2015	2014	
Collaboration and other research and development revenues	\$ 1,629	\$ —	\$ 1,629
Operating expenses:			
Research and development	18,846	5,073	13,773
General and administrative	18,095	7,650	10,445
Total operating expenses	36,941	12,723	24,218
Other expense, net:			
Other expense, net	(37,445)	(928)	(36,517)
Interest expense	(143)	(34)	(109)
Total other expense, net	(37,588)	(962)	(36,626)
Net loss	\$ (72,900)	\$ (13,685)	\$ (59,215)

*Collaboration and Other Research and Development Revenues*

Collaboration and other research and development revenue was \$1.6 million for the year ended December 31, 2015 and represented revenue recognized pursuant to our collaboration with Juno Therapeutics that we entered into in May 2015. We did not recognize any collaboration revenue in the year ended December 31, 2014.

*Research and Development Expenses*

Research and development expenses increased by \$13.8 million, to \$18.8 million for the year ended December 31, 2015 from \$5.1 million for the year ended December 31, 2014. The following table summarizes our research and development expenses for the years ended December 31, 2015 and December 31, 2014, together with the changes in those items in dollars (in thousands):

	Year Ended December 31,		Dollar Change
	2015	2014	
Employee and non-employee related expenses	\$ 8,203	\$ 1,894	\$ 6,309
Process and platform development expenses	3,957	874	3,083
License fees and expenses	4,603	1,202	3,401
Facility expenses	1,805	1,054	751
Other expenses	278	49	229
Total research and development expenses	\$ 18,846	\$ 5,073	\$ 13,773

The increase in research and development expenses was primarily attributable to:

- approximately \$6.3 million in increased research and development employee and non-employee, such as contractor and founder, compensation costs;
- approximately \$3.4 million in increased license fees and expenses due to sublicense payments that were triggered in the year ended December 31, 2015 under agreements with licensors as a result of our entry into our collaboration agreement with Juno Therapeutics;

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- approximately \$3.1 million in increased process and platform development costs;
- approximately \$0.8 million in increased facilities costs, including rent, utilities, and depreciation expense; and
- approximately \$0.2 million in increased other expenses.

### *General and Administrative Expenses*

General and administrative expenses increased by \$10.5 million, to \$18.1 million for the year ended December 31, 2015 from \$7.6 million for the year ended December 31, 2014. The increase in general and administrative expenses was primarily attributable to:

- approximately \$6.2 million in increased legal and patent-related fees, including third-party costs to procure the application for and issuance of additional patents in the United States and other jurisdictions; and
- approximately \$2.3 million in increased contractor consulting fees, \$1.8 million in increased employee compensation cost, and \$0.2 million in other general and administrative expenses.

### *Other Expense, Net*

Other expense, net was \$37.6 million for the year ended December 31, 2015 and \$1.0 million for the year ended December 31, 2014. The increase was primarily related to a \$35.6 million increase in our Series A preferred stock tranche right liability resulting from mark-to-market adjustments attributable to an increase in the fair value of our Series A preferred stock during 2015. The tranche right liability was settled in June 2015.

The increase in other expense, net was also attributable to a \$1.6 million mark-to-market adjustment recorded in June 2015 for the anti-dilution protection liability related to our issuance of common stock to our licensors. The anti-dilution liability was settled in June 2015.

## **Liquidity and Capital Resources**

### *Sources of Liquidity*

From inception through December 31, 2016, we funded our operations primarily through proceeds from private placements of our preferred stock of \$163.3 million, net proceeds from our IPO of \$97.5 million, an up-front payment, research and development payments and a milestone payment under our collaboration with Juno Therapeutics of \$25.0 million, \$4.8 million and \$2.5 million, respectively, \$2.0 million of gross proceeds from an equipment loan financing, and research and development payments from CFFT of \$0.3 million. As of December 31, 2016, we had cash and cash equivalents of \$185.3 million.

In addition to our existing cash and cash equivalents, we are eligible to earn milestone payments and are entitled to cost reimbursement under our collaboration agreement with Juno Therapeutics. Our ability to earn the milestone payments and cost reimbursements and the timing of earning these amounts are dependent upon the timing and outcome of our development, regulatory and commercial activities and are uncertain at this time. As of December 31, 2016, our right to payments under our collaboration agreement is our only committed potential external source of funds.

### *Indebtedness*

In May 2014, we entered into an equipment loan agreement with Silicon Valley Bank, which permitted us to borrow up to an aggregate principal amount of \$2.0 million. We borrowed \$0.5 million in July 2014, an additional



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\$0.8 million in January 2015, and \$0.7 million in July 2015. Each borrowing was payable in equal monthly principal installments over 36 months. In December 2015, we paid off all amounts outstanding under the loans and terminated the equipment loan agreement. In connection with the Silicon Valley Bank loans, we issued to Silicon Valley Bank a warrant to purchase up to 60,000 shares of our Series A-1 preferred stock at an exercise price of \$1.00 per share. The warrant had a 10 year term. Following a reverse stock split in January 2016 and the closing of our IPO in February 2016, such warrant converted into a warrant to purchase 23,076 shares of our common stock, which Silicon Valley Bank fully exercised pursuant to a net exercise provision for an aggregate of 19,271 shares of our common stock.

In December 2016, in connection with our entry into certain license agreements with Broad, we issued promissory notes, or the Notes, in an aggregate principal amount of \$10.0 million to Broad and Wageningen University, or Wageningen. Principal and interest on the Notes is payable in December 2017, or if earlier, a specified period of time following a company sale event. The Notes bear interest at a rate of 4.8% per annum. We may elect to make any payment of amounts outstanding under the Notes either in the form of cash or, subject to certain conditions, in shares of our common stock of equal value, with such shares being valued for such purpose at the closing price of our common stock as reported the NASDAQ Stock Market for the trading day immediately preceding the date of such payment if our common stock is then listed on the NASDAQ Stock Market. In the event of a change of control of our company or a sale of our company, we will be required to pay all remaining principal and accrued interest on the Notes in cash within a specified period following such event. Under the terms of the license agreement with Broad and Wageningen we may be required to issue additional promissory notes in connection with the achievement of success payment criteria. See “—Contractual Obligations” below for more information regarding such success payment criteria.

### *Cash Flows*

The following table provides information regarding our cash flows for the years ended December 31, 2016, 2015, and 2014, respectively (in thousands):

	2016	Year Ended December 31, 2015	2014
Net cash (used in) provided by:			
Operating activities	\$ (49,926)	\$ (5,403)	\$ (8,655)
Investing activities	(5,092)	(1,431)	(1,217)
Financing activities	97,161	139,391	18,483
Net increase in cash and cash equivalents	<u>\$ 42,143</u>	<u>\$ 132,557</u>	<u>\$ 8,611</u>

### *Net Cash Used in Operating Activities*

Net cash used in operating activities was \$49.9 million for the year ended December 31, 2016 compared to \$5.4 million for the year ended December 31, 2015. The increase of \$44.5 million in cash used in operating activities was primarily due to a decrease of \$37.2 million in non-cash expense from mark-to-market of our preferred stock tranche liability and anti-dilutive protection liability; a decrease of \$24.4 million in cash flows attributable to deferred revenue due to the receipt in 2015 of the \$25.0 million upfront payment under our collaboration with Juno Therapeutics; an increase of \$24.3 million in net loss; a decrease of \$0.6 million in cash flows attributable to prepaid expenses and other current assets; and other changes that net to \$0.2 million related to re-measurement of the warrant to purchase redeemable securities and other non-cash items. These decreases were partially offset by an increase of \$14.1 million in stock-based compensation expense and non-cash depreciation expense; an increase of \$13.0 million in cash flows attributable to accounts payable and accrued expenses; an increase of \$10.0 million from non-cash research and development expense; an increase of \$2.2 million in cash flows attributable to other non-current assets; a decrease in cash used attributable to accounts receivable of \$2.0 million; an increase of \$0.4 million in interest related to the facility lease obligation; and other changes that net to \$0.5 million related to deferred rent and changes in fair value of the warrant liability.

Net cash used in operating activities was \$5.4 million for the year ended December 31, 2015 compared to

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\$8.7 million of net cash used in operating activities for the year ended December 31, 2014. The decrease of \$3.3 million in cash used in operating activities was primarily due to an increase of \$36.5 million in non-cash expense from the mark to market of our preferred stock tranche liability, anti-dilutive protection liability, and warrant liability; an increase of \$25.3 million of deferred revenue under our collaboration with Juno Therapeutics during the year ended December 31, 2015; an increase of \$2.7 million in accrued expenses; and an increase of \$3.5 million and \$0.3 million in stock-based compensation expense and non-cash depreciation expense, respectively. These increases were partially offset by an increase in net loss of \$59.2 million, a decrease in cash flows attributable to accounts receivable and prepaid expenses and other current assets of \$1.3 million, a decrease in accounts payable of \$3.6 million, and other changes that net to \$0.9 million related to deferred rent, non-cash loss on extinguishment of debt and research and development expenses.

### *Net Cash Used in Investing Activities*

Net cash used in investing activities was \$5.1 million for the year ended December 31, 2016 compared to \$1.4 million for the year ended December 31, 2015. The increase in cash used in investing activities was primarily attributable to an increase for the acquisition of property, plant and equipment and an increase in restricted cash related to our letter of credit for our new facility lease at Hurley Street.

Net cash used in investing activities was \$1.4 million for the year ended December 31, 2015, compared to \$1.2 million for the year ended December 31, 2014. The increase of \$0.2 million in cash used in investing activities was due to purchases of laboratory equipment.

### *Net Cash Provided by Financing Activities*

Net cash provided by financing activities was \$97.2 million for the year ended December 31, 2016, compared to \$139.4 million for the year ended December 31, 2015. The decrease of \$42.2 million in cash provided by financing activities was primarily related to the Company receiving less proceeds in 2016 compared to 2015. In 2015, we received proceeds of \$141.7 million related to the issuance of Series A-2 and Series B preferred stock and received proceeds of \$1.5 million from our equipment loan, compared to proceeds of \$97.5 million from our IPO in 2016. This decrease was partially offset by higher payments in 2015, specifically a \$2.0 million payment for our equipment loan and a \$1.7 million payment for fees related to our IPO, compared to a \$0.6 million payment in 2016 for our constructing financing obligation. The remaining differences relates to proceeds from stock exercises and the payment of the final fee of our loan payment.

Net cash provided by financing activities was \$139.4 million for the year ended December 31, 2015, compared to \$18.5 million for the year ended December 31, 2014. The increase of \$120.9 million in cash provided by financing activities was primarily due to the issuance of Series A-2 and Series B preferred stock, net of issuance costs, in 2015, resulting in an increase in aggregate gross proceeds of \$123.7 million during the year ended December 31, 2015, and proceeds from an increase in borrowings under the equipment loan of \$1.0 million. This increase was partially offset by payoff of the equipment loan of \$2.1 million and the payment of deferred initial public offering costs of \$1.7 million.

### *Funding Requirements*

We expect our expenses to increase in connection with our ongoing activities, particularly as we further advance our current research programs and our preclinical development activities; seek to identify product candidates and additional research programs; initiate preclinical testing and clinical trials for any product candidates we identify and develop; maintain, expand, and protect our intellectual property portfolio; hire additional clinical, quality control, and scientific personnel; and incur additional costs associated with operating as a public company. In addition, if we obtain marketing approval for any product candidate that we identify and develop, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution to the extent that such sales, marketing, and distribution are not the responsibility of a collaborator. We do not expect to generate significant recurring revenue unless and until we obtain regulatory approval for and commercialize a product candidate. Furthermore, following the closing of our IPO, we have begun to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing

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operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, or eliminate our research and development programs or future commercialization efforts.

We expect that our existing cash and cash equivalents at December 31, 2016, anticipated interest income, anticipated research support under our collaboration agreement with Juno Therapeutics, anticipated payments from CFFT, and anticipated payments from our subtenant will enable us to fund our operating expenses and capital expenditure requirements for at least the next 18 months following the date of this Annual Report on Form 10-K. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the scope, progress, results, and costs of drug discovery, preclinical development, laboratory testing, and clinical trials for the product candidates we may develop;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights, and defending intellectual property-related claims;
- the costs, timing, and outcome of regulatory review of the product candidates we may develop;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing, and distribution, for any product candidates for which we receive regulatory approval;
- the success of our collaboration with Juno Therapeutics;
- whether Juno Therapeutics exercises either or both of its options to extend the research program term under our collaboration (each of which would trigger an extension payment to us);
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the extent to which we acquire or in-license other medicines and technologies;
- the costs of reimbursing our licensors for the prosecution and maintenance of the patent rights in-licensed by us; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive, and uncertain process that takes many years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, any product candidate that we identify and develop, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of genomic medicines that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt 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 raise funds through additional collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional

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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.

### Contractual Obligations

The following table summarizes our significant contractual obligations as of payment due date by period at December 31, 2016 (in thousands):

	Total	Less Than			More than
		1 Year	1 to 3 Years	3 to 5 Years	5 Years
Notes payable <sup>(1)</sup>	10,500	10,500	—	—	—
Operating lease obligations	29,057	3,957	12,467	8,832	3,801
Total	<u>\$ 39,557</u>	<u>\$ 14,457</u>	<u>\$ 12,467</u>	<u>\$ 8,832</u>	<u>\$ 3,801</u>

- (1) The Notes are convertible, at our option, into shares of our common stock subject to certain conditions. In the event of a change of control of our company or a sale of our company, we will be required to pay all remaining principal and accrued interest on the Notes in cash within a specified period following such event.

The table above does not include potential milestone and success fees, sublicense fees, royalty fees, licensing maintenance fees, and reimbursement of patent maintenance costs that we may be required to pay under agreements we have entered into with certain institutions to license intellectual property. Our agreements to license intellectual property include potential milestone payments that are dependent upon the development of products using the intellectual property licensed under the agreements and contingent upon the achievement of development or regulatory approval milestones, as well as commercial milestones. We have not included such potential obligations in the table above because they are contingent upon the occurrence of future events and the timing and likelihood of such potential obligations are not known with certainty. For further information regarding these agreements, please see “Business—License Agreements.”

Pursuant to the license agreement with respect to Cas9 that we entered into with Broad and Harvard in October 2014, as amended and restated in December 2016 and as further amended in March 2017, which we refer to as the Cas9-I License Agreement, the license agreement with respect to Cpfl that we entered into with Broad in December 2016, or the Cpfl License Agreement, and the license agreement with respect to Cas9 that we entered into the Broad in December 2016, or the Cas9-II License Agreement, we have incurred an aggregate of \$23.1 million, \$9.4 million and \$1.7 million in expense during the years ended December 31, 2016, 2015 and 2014, respectively, for reimbursement of expenses associated with the prosecution and maintenance of the patents and patent applications licensed to us under such license agreements, including expenses associated with any interference proceedings in the United States Patent and Trademark Office, any opposition proceedings in the European Patent Office or any other *inter partes* or other post grant proceedings in these or other jurisdictions where we are seeking patent protection (described in more detail in “Business—License Agreements”). Given the interference and opposition proceedings involving the patents licensed to us under the Cas9-I License Agreement are ongoing (described in more detail under “—Legal Proceedings” in Part I, Item 3 of this Annual Report on Form 10-K), we anticipate that our obligation to reimburse Broad and Harvard under the Cas9-I License Agreement for these expenses during future periods will be substantial until such interference and opposition proceedings are resolved.

Under the Cas9-I License Agreement, Broad and Harvard are collectively entitled to receive clinical and regulatory milestone payments totaling up to \$14.8 million in the aggregate per licensed product approved in the United States, the European Union, and Japan for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. If we undergo a change of control during the term of this license agreement, these clinical and regulatory milestone payments will be increased by a certain percentage in the mid double-digits. We are also obligated to make additional payments to Broad and Harvard, collectively, of up to an aggregate of \$54.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or

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treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. Broad and Harvard are collectively entitled to receive clinical and regulatory milestone payments totaling up to \$4.1 million in the aggregate per licensed product approved in the United States and at least one jurisdiction outside the United States for the prevention or treatment of a human disease that afflicts fewer than a specified number of patients in the aggregate in the United States or a specified number of patients per year in the United States, which we refer to as an ultra-orphan disease. We are also obligated to make additional payments to Broad and Harvard, collectively, of up to an aggregate of \$36.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or treatment of an ultra-orphan disease.

Under the Cpfl License Agreement, Broad and Wageningen are collectively entitled to receive clinical and regulatory milestone payments totaling up to \$20.0 million in the aggregate per licensed product approved in the United States, the European Union and Japan for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. If we undergo a change of control during the term of the Cpfl License Agreement, certain of these clinical and regulatory milestone payments will be increased by a certain percentage in the mid double-digits. We are also obligated to make additional payments to Broad and Wageningen, collectively, of up to an aggregate of \$54.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. Broad and Wageningen are collectively entitled to receive clinical and regulatory milestone payments totaling up to \$6.0 million in the aggregate per licensed product approved in the United States, the European Union and Japan for the prevention or treatment of an ultra-orphan disease. We are also obligated to make additional payments to Broad and Wageningen, collectively, of up to an aggregate of \$36.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or treatment of an ultra-orphan disease.

Under the Cas9-II Agreement, we are obligated to pay clinical and regulatory milestone payments per licensed product approved in the United States, European Union and Japan for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States totaling up to \$3.7 million in the aggregate, and the sales milestone payments for any such licensed product totaling up to \$13.5 million in the aggregate and clinical and regulatory milestone payments totaling up to \$1.1 million in the aggregate per licensed product approved in the United States and the European Union or Japan for the prevention or treatment of a human disease that afflicts fewer than a specified number of patients in the United States, plus sales milestone payments of up to \$9.0 million for any such licensed product.

Under the Cpfl License Agreement, Broad and Wageningen are also entitled, collectively, to receive success payments in the event our market capitalization reaches specified thresholds ascending from a high nine digit dollar amount to \$10.0 billion, or Cpfl Market Cap Success Payments, or sale of our company for consideration in excess of those thresholds, or Cpfl Company Sale Success Payments, which, collectively with the Cpfl Market Cap Success Payments, we refer to as the Cpfl Success Payments. The Cpfl Success Payments that may be paid to Broad and Wageningen range from a mid seven digit dollar amount to a mid eight digit dollar amount, and collectively will not exceed, in aggregate, \$125.0 million, which maximum would be payable only if we achieve a market capitalization threshold of \$10.0 billion and have at least one product candidate covered by a specified claim of a patent right licensed to us or was the subject of a clinical trial pursuant to development efforts by us or any of our affiliates or sublicensees. Under the Cas9-II Agreement, Broad is entitled to receive similar market cap success payments and company sale success payments in the event our market capitalization reaches specified thresholds ascending from a low ten digit dollar amount to \$9.0 billion, which we refer to as the Cas9-II Success Payments. The Cas9-II Success Payments range from a low seven digit dollar amount to a low eight digit dollar amount and that will not exceed, in aggregate, \$30.0 million, which maximum would be owed only if we reach a market capitalization threshold of \$9.0 billion and have at least one product candidate covered by a claim of a patent right licensed to us under either the Cas9-II License Agreement or the Cas9-I License Agreement that is or was the subject of a clinical trial pursuant to development efforts by us or any of our affiliates or sublicensees. Market cap success payments are payable by us in cash or in the form of promissory notes on substantially the same terms and conditions as the Notes, except that the maturity date of such notes will, subject to certain exceptions, be 150 days following issuance. Following a change in control of our company, market cap success payments are required to be made in cash. Company sale success payments are payable solely in cash.

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Under the exclusive patent license agreement we entered into in August 2016 with MGH, or the Second License MGH Patent Rights, we are required to pay annual license fees and make clinical and regulatory milestone payments totaling less than \$1 million in the aggregate for up to four licensed products or processes upon achievement of specified clinical and regulatory milestones and commercial sales milestone payments totaling up to \$4.9 million in the aggregate upon the achievement of milestones relating to the first commercial sales of up to four licensed products or processes, as well as milestones relating to annual net sales of products or processes meeting specified thresholds. We are also obligated to reimburse MGH for all patent costs and future reasonable costs associated with the prosecution, filing, and maintenance of the licensed patents. Under the Second MGH License Agreement, MGH is also entitled to receive certain payments in the event our market capitalization reaches specified thresholds ascending from the low ten digit dollar amount to \$9.0 billion, or MGH Market Cap Success Payments. The MGH Market Cap Success Payments payable to MGH range from a low seven digit dollar amount to a low eight digit dollar amount, and will not exceed \$24.0 million in the aggregate, which maximum would be payable only if we achieve a market capitalization of \$9.0 billion and if we have one licensed product that meets certain specified clinical or regulatory milestones. In addition, in the event of an asset sale or merger of our company to a third party for consideration in excess of one or more market capitalization thresholds, we must pay MGH all MGH Market Cap Success Payments corresponding to such market capitalization thresholds that have not previously been paid.

Under each of our license agreements with MGH and Broad, we also may be obligated to pay royalties of low single digit to low double digits as a percentage of net product sales depending on the terms of the applicable agreement.

If we achieve a market capitalization thresholds ranging from a mid to high nine digit dollar amount to a low ten digit dollar amount for a specified period of time or we sell our company for consideration in excess of such thresholds, then we are obligated under the Cpfl License Agreement, the Cas-9 II License Agreement, and the Second MGH License Agreement to collectively pay success payments in an aggregate of up to a mid-teen million dollar amount to our licensors. Success payments are payable only once as either market capitalization success payments or company sale success payments. Additionally, if we terminate the Cpfl License Agreement, Cas-9 II License Agreement, and Second MGH License Agreement prior to achieving a market capitalization or company sale threshold, we have no obligation to make any success payments.

Under the terms of our collaboration with Juno Therapeutics, we received an upfront payment of \$25.0 million from Juno Therapeutics in the second quarter of 2015. In addition, we are eligible to receive research support of up to \$22.0 million over a five year term and across the three programs under the collaboration, subject to adjustment in accordance with the terms of the collaboration, of which, we had recognized \$4.8 million as of December 31, 2016.

We enter into contracts in the normal course of business with contract research organizations, or CROs, to assist in the performance of our research and development activities and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

### **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 applicable Securities and Exchange Commission rules.

### ***JOBS Act***

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an “emerging growth company,” or EGC, may take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. Thus, an EGC is permitted to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

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We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an EGC, we intend to rely on certain of these exemptions, including without limitation, (1) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (2) complying with any requirement that may be adopted by the Public Company Accounting Oversight Board, or PCAOB, regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an EGC until the earlier of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1.0 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the completion of our IPO; (iii) the date on which we have issued more than \$1.0 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.

**Item 7A. Quantitative and Qualitative Disclosures About Market Risk.**

We are exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments, including cash equivalents, are in the form, or may be in the form of, money market funds or marketable securities and are or may be invested in U.S. Treasury and U.S. government agency obligations. Due to the short-term maturities and low risk profiles 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 investments.

We are not currently exposed to market risk related to changes in foreign currency exchange rates; however, we may contract with vendors that are located in Asia and Europe in the future and may be subject to fluctuations in foreign currency rates at that time.

Inflation would generally affect us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2016, 2015 and 2014.



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**Item 8. Financial Statement and Other Supplementary Information.**

**EDITAS MEDICINE, INC.**

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**Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders of  
Editas Medicine, Inc.

We have audited the accompanying consolidated balance sheets of Editas Medicine, Inc. (the “Company”) as of December 31, 2016 and 2015, and the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders’ equity (deficit), and cash flows for each of the three years in the period ended December 31, 2016. These consolidated financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on these consolidated 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 consolidated financial statements are free of material misstatement. We were not engaged to perform an audit of the Company’s internal control over financial reporting. Our audits 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, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the consolidated financial position of Editas Medicine, Inc. at December 31, 2016 and 2015, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts  
March 3, 2017

**Editas Medicine, Inc.**  
**Consolidated Balance Sheets**  
(amounts in thousands, except share and per share data)

	December 31,	
	2016	2015
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$ 185,323	\$ 143,180
Accounts receivable	88	1,019
Prepaid expenses and other current assets	1,772	786
Total current assets	<u>187,183</u>	<u>144,985</u>
Property and equipment, net	40,378	2,130
Restricted cash and other non-current assets	1,621	2,248
Total assets	<u>\$ 229,182</u>	<u>\$ 149,363</u>
<b>LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)</b>		
Current liabilities:		
Accounts payable	\$ 4,640	\$ 1,381
Accrued expenses	17,439	5,456
Notes payable	10,000	—
Deferred rent, current portion	18	88
Other current liabilities	986	—
Total current liabilities	<u>33,083</u>	<u>6,925</u>
Deferred rent, net of current portion	380	—
Deferred revenue, net of current portion	26,000	25,321
Warrant to purchase redeemable securities	—	289
Construction financing lease obligation, net of current portion	35,096	—
Other non-current liabilities	16	27
Total liabilities	<u>94,575</u>	<u>32,562</u>
Commitments and contingencies (see note 7)		
Series A-1 redeemable convertible preferred stock, \$0.0001 par value per share: no shares and 21,320,000 shares authorized at December 31, 2016 and December 31, 2015, respectively; no shares and 21,260,000 shares issued and outstanding at December 31, 2016 and December 31, 2015, respectively	—	21,137
Series A-2 redeemable convertible preferred stock, \$0.0001 par value per share: no shares and 16,890,699 shares authorized, issued and outstanding at December 31, 2016 and December 31, 2015, respectively	—	59,027
Series B redeemable convertible preferred stock, \$0.0001 par value per share: no shares and 26,666,660 shares authorized, issued and outstanding at December 31, 2016 and December 31, 2015, respectively	—	119,751
Stockholders' equity (deficit)		
Preferred stock, \$0.0001 par value per share: 5,000,000 shares and no shares authorized, at December 31, 2016 and December 31, 2015, respectively; no shares issued or outstanding at December 31, 2016 and December 31, 2015, respectively	—	—
Common stock, \$0.0001 par value per share: 195,000,000 shares and 92,000,000 shares authorized at December 31, 2016 and December 31, 2015, respectively; 36,662,724 and 4,869,829 shares issued and 35,818,131 and 3,233,638 shares outstanding at December 31, 2016 and December 31, 2015, respectively	4	—
Additional paid-in capital	320,129	5,234
Accumulated deficit	(185,526)	(88,348)
Total stockholders' equity (deficit)	<u>134,607</u>	<u>(83,114)</u>
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	<u>\$ 229,182</u>	<u>\$ 149,363</u>

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

**Editas Medicine, Inc.**  
**Consolidated Statements of Operations and Comprehensive Loss**  
**(amounts in thousands, except per share and share data)**

	2016	Year Ended December 31, 2015	2014
Collaboration and other research and development revenues	\$ 6,053	\$ 1,629	\$ —
Operating expenses:			
Research and development	56,979	18,846	5,073
General and administrative	46,262	18,095	7,650
Total operating expenses	103,241	36,941	12,723
Operating loss	(97,188)	(35,312)	(12,723)
Other income (expense), net			
Other expense, net	(57)	(37,445)	(928)
Interest income (expense), net	62	(143)	(34)
Total other income (expense), net	5	(37,588)	(962)
Net loss and comprehensive loss	\$ (97,183)	\$ (72,900)	\$ (13,685)
Reconciliation of net loss to net loss attributable to common stockholders:			
Net loss	\$ (97,183)	\$ (72,900)	\$ (13,685)
Accretion of redeemable convertible preferred stock to redemption value	(47)	(394)	(309)
Net loss attributable to common stockholders	\$ (97,230)	\$ (73,294)	\$ (13,994)
Net loss per share attributable to common stockholders, basic and diluted	\$ (3.02)	\$ (28.55)	\$ (12.46)
Weighted-average common shares outstanding, basic and diluted	32,219,717	2,566,916	1,123,098

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

**Editas Medicine, Inc.**  
**Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)**  
**(amounts in thousands except share data)**

	Series A-1 Redeemable Convertible Preferred Stock		Series A-2 Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' (Deficit) Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
<b>Balance at December 31, 2013</b>	3,260,000	2,111	—	—	—	—	751,200	—	—	(1,763)	(1,763)
Issuance of common stock to licensors	—	—	—	—	—	—	628,379	—	408	—	408
Issuance of Series A-1 redeemable convertible preferred stock, net of issuance costs of \$20	18,000,000	17,980	—	—	—	—	—	—	—	—	—
Reclassification of tranche rights upon issuance of redeemable convertible preferred stock	—	372	—	—	—	—	—	—	7	—	7
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—
Vesting of restricted common stock and common stock subject to repurchase	—	—	—	—	—	—	77,942	—	2	—	2
Vesting of founder shares	—	—	—	—	—	—	405,648	—	48	—	48
Accretion of redeemable convertible preferred stock to redemption value	—	309	—	—	—	—	—	—	(309)	—	(309)
Net loss	—	—	—	—	—	—	—	—	—	(13,685)	(13,685)
<b>Balance at December 31, 2014</b>	21,260,000	20,772	—	—	—	—	1,863,169	—	156	(15,448)	(15,292)
Issuance of Series A-2 redeemable convertible preferred stock, net of issuance costs of \$1	—	—	16,890,699	21,989	—	—	—	—	—	—	—
Reclassification of tranche rights upon issuance of redeemable convertible preferred stock	—	—	—	37,038	—	—	—	—	—	—	—
Issuance of Series B redeemable convertible preferred stock, net of issuance costs of \$278	—	—	—	—	26,666,660	119,722	—	—	—	—	—
Accretion of redeemable convertible preferred stock to redemption value	—	365	—	—	—	29	—	—	(394)	—	(394)
Issuance of common stock to licensors upon settlement of anti-dilution protection liability	—	—	—	—	—	—	327,970	—	1,936	—	1,936
Exercise of stock options	—	—	—	—	—	—	28,651	—	6	—	6
Vesting of restricted common stock and common stock subject to repurchase	—	—	—	—	—	—	653,272	—	17	—	17
Vesting of founder shares	—	—	—	—	—	—	360,576	—	2,345	—	2,345
Stock-based compensation expense	—	—	—	—	—	—	—	—	1,168	—	1,168
Net loss	—	—	—	—	—	—	—	—	—	(72,900)	(72,900)
<b>Balance at December 31, 2015</b>	21,260,000	\$ 21,137	16,890,699	\$ 59,027	26,666,660	\$ 119,751	3,233,638	\$ —	\$ 5,234	\$ (88,348)	\$ (83,114)
Accretion of redeemable convertible preferred stock to redemption value	—	40	—	—	—	7	—	—	(47)	—	(47)
Conversion of redeemable convertible preferred stock into common stock upon closing of the initial public offering	(21,260,000)	(21,177)	(16,890,699)	(59,027)	(26,666,660)	(119,758)	24,929,709	3	199,954	5	199,962
Conversion of preferred stock warrant to common stock warrant upon closing of initial public offering	—	—	—	—	—	—	—	—	376	—	376
Issuance of common stock from initial public offering, net of issuance costs of \$11.1 million	—	—	—	—	—	—	6,785,000	1	97,487	—	97,488
Exercise of common stock warrant	—	—	—	—	—	—	19,271	—	—	—	—
Exercise of stock options	—	—	—	—	—	—	58,915	—	233	—	233
Vesting of restricted common stock and common stock subject to repurchase	—	—	—	—	—	—	431,018	—	11	—	11
Vesting of founder shares	—	—	—	—	—	—	360,580	—	8,315	—	8,315
Stock-based compensation expense	—	—	—	—	—	—	—	—	8,566	—	8,566
Net loss	—	—	—	—	—	—	—	—	—	(97,183)	(97,183)
<b>Balance at December 31, 2016</b>	—	\$ —	—	\$ —	—	\$ —	35,818,131	\$ 4	\$ 320,129	\$ (185,526)	\$ 134,607

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

**Editas Medicine, Inc.**  
**Consolidated Statements of Cash Flows**

	Year Ended December 31,		
	2016	2015	2014
<b>Cash flow from operating activities</b>			
Net loss	\$ (97,183)	\$ (72,900)	\$ (13,685)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	16,881	3,513	55
Depreciation	1,202	471	157
Changes in fair value of warrant liability	87	—	—
Interest related to facility lease obligation	445	—	—
Non-cash research and development expenses	10,000	—	730
Re-measurement of warrant to purchase redeemable securities	—	241	(2)
Change in fair value of preferred stock tranche asset or liability	—	35,551	938
Changes in fair value of anti-dilutive protection liability	—	1,609	5
Changes in deferred rent	310	(96)	184
Other non-cash items, net	114	149	19
Changes in operating assets and liabilities:			
Accounts receivable	931	(1,019)	—
Prepaid expenses and other current assets	(986)	(373)	(88)
Other non-current assets	2,246	40	(20)
Accounts payable	3,251	(1,436)	2,191
Accrued expenses	11,841	3,526	861
Deferred revenue	935	25,321	—
Net cash used in operating activities	<u>(49,926)</u>	<u>(5,403)</u>	<u>(8,655)</u>
<b>Cash flow from investing activities</b>			
Purchases of property and equipment	(3,493)	(1,431)	(1,217)
Proceeds from the sale of equipment	20	—	—
Changes in restricted cash	(1,619)	—	—
Net cash used in investing activities	<u>(5,092)</u>	<u>(1,431)</u>	<u>(1,217)</u>
<b>Cash flow from financing activities</b>			
Proceeds from equipment loan, net of issuance costs	—	1,500	462
Proceeds from initial public offering of common stock, net of issuance costs	97,488	—	—
Proceeds from exercise of stock options	233	—	—
Payments on construction financing lease obligation	(560)	—	—
Proceeds from the issuance of redeemable convertible preferred stock and tranche rights, net of issuance costs	—	141,711	17,980
Payments of equipment loan principal	—	(2,000)	—
Payments of final fee for loan payoff	—	(80)	—
Proceeds from the issuance of common stock and restricted stock	—	6	41
Payments of initial public offering costs	—	(1,746)	—
Net cash provided by financing activities	<u>97,161</u>	<u>139,391</u>	<u>18,483</u>
Net increase in cash and cash equivalents	42,143	132,557	8,611
Cash and cash equivalents, beginning of period	143,180	10,623	2,012
Cash and cash equivalents, end of period	<u>\$ 185,323</u>	<u>\$ 143,180</u>	<u>\$ 10,623</u>
<b>Supplemental disclosure of cash and non-cash activities:</b>			
Accretion of redeemable convertible preferred stock to redemption value	\$ 47	\$ 394	\$ 309
Fixed asset additions included in accounts payable and accrued expenses	130	58	—
Construction financing lease obligation	35,941	—	—
Conversion of anti-dilutive protection liability to common stock	—	1,936	—
Reclassification of warrants to additional paid in capital	376	—	—
Conversion of preferred stock to common stock upon closing of the initial public offering	199,962	—	—
Reclassification of liability for common stock subject to repurchase	11	17	2
Accrual of final payment fee on equipment loan and debt discount	—	—	20
Interest Paid	465	91	—
Initial public offering costs incurred but unpaid at period end	—	502	—
Reclassification of preferred stock tranche liability upon settlement	—	37,038	372

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

**Editas Medicine, Inc.**  
**Notes to Consolidated Financial Statements**

**1. Nature of Business**

Editas Medicine, Inc. (the “Company”) is a research stage company dedicated to treating patients with genetically defined diseases by correcting their disease-causing genes. The Company was incorporated in the state of Delaware in September 2013. Its principal offices are in Cambridge, Massachusetts.

Since its inception, the Company has devoted substantially all of its efforts to business planning, research and development, recruiting management and technical staff, and raising capital, and has financed its operations through various equity and debt financings, including the initial public offering of its common stock (“IPO”), private placements of preferred stock and an equipment loan, and from upfront, milestone and research and development fees paid under a research collaboration with Juno Therapeutics, Inc. (“Juno Therapeutics”), and from research and development payments from the Cystic Fibrosis Foundation Therapeutics, Inc. (“CFFT”), a non-profit drug discovery and development affiliate of the Cystic Fibrosis Foundation.

The Company is subject to risks common to companies in the biotechnology industry, including but not limited to, risks of failure of preclinical studies and clinical trials, the need to obtain marketing approval for any drug product candidate that it may identify and develop, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations and ability to transition from pilot-scale manufacturing to large-scale production of products.

***Liquidity***

In February 2016, the Company completed its IPO whereby the Company sold 6,785,000 shares of its common stock, inclusive of 885,000 shares of common stock sold by the Company pursuant to the full exercise of an overallotment option granted to the underwriters in connection with the offering, at a price to the public of \$16.00 per share. The shares began trading on the NASDAQ Global Select Market on February 3, 2016. The aggregate net proceeds received by the Company from the offering were \$97.5 million, after deducting underwriting discounts and commissions and other offering expenses payable by the Company. In connection with the IPO, the board of directors and the stockholders of the Company approved a one-for-2.6 reverse stock split of the Company’s issued and outstanding common stock. The reverse stock split became effective on January 15, 2016. All share and per share amounts in the consolidated financial statements have been retroactively adjusted for all periods presented to give effect to the reverse stock split, including reclassifying an amount equal to the reduction in par value to additional paid-in capital. Upon the closing of the IPO, all outstanding shares of convertible preferred stock converted into 24,929,709 shares of common stock. As of December 31, 2016, there were 35,818,131 shares of common stock outstanding. The significant increase in shares outstanding in the first quarter of 2016 is expected to impact the year-over-year comparability of the Company’s net loss per share calculations for the next three months.

The Company has incurred annual net operating losses in every year since its inception. The Company expects that its existing cash and cash equivalents at December 31, 2016, anticipated interest income, anticipated research support under the Company’s collaboration agreement with Juno Therapeutics, anticipated payments from CFFT, and anticipated payments from the Company’s subtenant will enable it to fund its operating expenses and capital expenditure requirements for at least the next 18 months following the date of this Annual Report on Form 10-K. The Company will require substantial additional capital to fund operations beyond this date. The Company has not generated any product revenues and has financed its operations primarily through public offerings and private placements of its equity securities, and funding from its collaboration with Juno Therapeutics. There can be no assurance that the Company will be able to obtain additional debt or equity financing or generate product revenue or revenues from collaborative partners, on terms acceptable to the Company, on a timely basis or at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company’s business, results of operations, and financial condition.



## 2. Summary of significant accounting policies

### *Principles of Consolidation*

The accompanying consolidated financial statements include the accounts of Editas Medicine, Inc. and its wholly owned subsidiary, Editas Securities Corporation, which is a Delaware subsidiary created to buy, sell and hold securities. All intercompany transactions and balances have been eliminated.

### *Basis of Presentation*

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (“GAAP”). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Updates (“ASU”) of the Financial Accounting Standards Board (“FASB”).

### *Use of Estimates*

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. On an ongoing basis, the Company’s management evaluates its estimates, which include, but are not limited to, estimates related to revenue recognition, accrued expenses, stock-based compensation expense, valuation of the redeemable convertible preferred stock tranche liability and the anti-dilutive protection liability, valuation of the warrant liability, deferred tax valuation allowances, the fair value of common stock prior to the completion of the IPO, and the construction lease financing obligation. The Company bases its estimates on historical experience and other market-specific or relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

### *Fair Value of Financial Instruments*

ASC Topic 820, *Fair Value Measurement* (“ASC 820”), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company’s own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company’s assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- *Level 1* – Quoted market prices in active markets for identical assets or liabilities.
- *Level 2* – Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted market prices, interest rates, and yield curves.
- *Level 3* – Unobservable inputs developed using estimates of assumptions developed by the Company, which reflect those that a market participant would use.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument’s level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

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The carrying amounts reflected in the consolidated balance sheets for cash and cash equivalents, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values, due to their short-term nature.

***Cash and Cash Equivalents***

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents. Cash and cash equivalents include cash held in banks and amounts held in money market funds.

***Restricted Cash***

The Company had restricted cash of \$1.6 million and \$0.3 million held in the form of money market accounts as collateral for the Company's facility lease obligation as of December 31, 2016 and 2015, respectively. The restricted cash balance is included within restricted cash and other non-current assets and other current assets in the accompanying consolidated balance sheets at December 31, 2016 and 2015, respectively.

***Accounts Receivable***

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding invoices and the overall quality and age of those invoices not specifically reviewed. The Company's receivables primarily relate to amounts reimbursed under its collaboration agreement. The Company believes that credit risks associated with its collaborations partner is not significant. To date, the Company has not had any write-offs of bad debt, and the Company did not have an allowance for doubtful accounts as of December 31, 2016 and 2015.

***Property and Equipment***

Property and equipment consists of computers, laboratory equipment, furniture and office equipment, and leasehold improvements and is stated at cost, less accumulated depreciation. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred, while costs of major additions and betterments are capitalized. Depreciation is calculated over the estimated useful lives of the assets using the straight-line method. The Company capitalizes laboratory equipment used for research and development if it has alternative future use in research and development or otherwise.

<b>Asset:</b>	<b>Estimated Useful life</b>
Lab equipment	5 years
Computer equipment and software	3 years
Furniture and equipment	5 years
Leasehold improvements	Shorter of useful life or remaining lease term
Building	30 years

***Impairment of Long-lived Assets***

The Company evaluates long-lived assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book values of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book values of the assets exceed their fair value. The Company has not recognized any impairment losses from inception through December 31, 2016.

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### **Revenue Recognition**

To date, the Company has earned revenue under the collaboration and license agreement with Juno Therapeutics and its award agreement with CFFT (see Note 8).

The Company recognizes revenue in accordance with ASC Topic 605, *Revenue Recognition* ("ASC 605"). Accordingly, revenue is recognized 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.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified in current liabilities. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

The Company evaluates multiple-element arrangements based on the guidance in ASC Topic 605-25, *Revenue Recognition Multiple-Element Arrangements* ("ASC 605-25"). Pursuant to the guidance in ASC 605-25, the Company evaluates multiple-element arrangements to determine (1) the deliverables included in the arrangement and (2) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and 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 the delivered item has value to the customer on a standalone basis and, if the arrangement includes a general right of return relative 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 a 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.

Options are considered substantive if, at the inception of the arrangement, the Company is at risk as to whether the collaboration partner will choose to exercise the option. Factors that the Company considers in evaluating whether an option is substantive include the cost to exercise the option, the overall objective of the arrangement, the benefit the collaborator might obtain from the arrangement without exercising the option and the likelihood the option will be exercised. When an option is considered substantive, the Company does not consider the option or item underlying the option to be a deliverable at the inception of the arrangement and the associated option fees are not included in allocable consideration, assuming the option is not priced at a significant and incremental discount. Conversely, when an option is not considered substantive, the Company would consider the option, including other deliverables contingent upon the exercise of the option, to be a deliverable at the inception of the arrangement and a corresponding amount would be included in allocable arrangement consideration. In addition, if the price of the option includes a significant incremental discount, the discount would be included as a deliverable at the inception of the arrangement.

The consideration received under the arrangement that is fixed or determinable is then allocated among the separate units of accounting using the relative selling price method. The Company determines the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence ("VSOE") of selling price, if available, third-party evidence ("TPE") of selling price if VSOE is not available, or best estimate of selling price ("BESP") if neither VSOE nor TPE is available. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, the Company considers applicable market conditions and

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relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company validates the BEBP for units of accounting by evaluating whether changes in the key assumptions used to determine the BEBP 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 in ASC 605 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 Company's contractual or estimated performance period for the undelivered elements, 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 in 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.

At the inception of an arrangement that includes milestone payments, 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: (1) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from its performance to achieve the milestone, (2) the consideration relates solely to past performance and (3) 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. Milestones that are not considered substantive are recognized as earned if there are no remaining performance obligations or over the remaining period of performance, assuming all other revenue recognition criteria are met.

The Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

### ***Research and Development Costs***

Research and development costs are charged to expense as incurred in performing research and development activities. The costs include employee-related expenses including salaries, benefits, and stock-based compensation expense, costs of funding research performed by third parties that conduct research and development and preclinical activities on the Company's behalf, the cost of purchasing lab supplies and non-capital equipment used in preclinical activities, consultant fees, facility costs including rent, depreciation, and maintenance expenses, and fees for acquiring and maintaining licenses under third party licensing agreements. The Company defers and capitalizes non-refundable advance payments made by the Company for research and development activities until the related goods are received or the related services are performed. In circumstances where amounts have been paid in excess of costs incurred, the Company records a prepaid expense.

### ***Patent Costs***

The Company expenses patent and patent application costs and related legal costs for the prosecution and maintenance of such patents and patent applications, including patents and patent applications the Company licenses, as incurred and classifies such costs as general and administrative expenses in the accompanying statements of operations.

***Construction Financing Lease Obligation***

Beginning in 2016, the Company began recording certain estimated construction costs incurred and reported to the Company by a landlord as an asset and corresponding construction financing lease obligation on the Company's consolidated balance sheets because it was deemed to be the owner of the building during the construction period for accounting purposes. In each reporting period, the landlord estimated and reported to the Company the costs incurred to date and provided supporting invoices for the Company to review. The Company periodically met with the landlord and its construction manager to review the estimates and observe construction progress prior to recording such amounts. Construction was completed in October 2016 and the Company considered the requirements for sale-leaseback accounting treatment, which included an evaluation of whether all risks of ownership had transferred back to the landlord as evidenced by a lack of continuing involvement in the lease property. The Company determined that the arrangement did not qualify for sale lease-back accounting treatment, the building asset will remain on the Company's balance sheet at its historical cost, and such asset would be depreciated over its estimated useful life of thirty years.

***Warrants to Purchase Convertible Preferred Stock***

In conjunction with an equipment loan financing, the Company issued to Silicon Valley Bank a warrant to purchase up to 60,000 shares of the Company's Series A-1 preferred stock at an exercise price of \$1.00 per share. The fair value of the warrant at the issuance date was recorded as a reduction to face value of the debt balance and was amortized as interest expense, along with other debt issuance costs, over the term of the loan. Due to the liquidation preferences of the Series A-1 preferred stock, the Company recorded the warrant as a liability on the consolidated balance sheets. Following a reverse stock split in January 2016 and the closing of the IPO in February 2016, such warrant converted into a warrant to purchase 23,076 shares of common stock, which Silicon Valley Bank fully exercised in February 2016 pursuant to a net exercise provision for an aggregate of 19,271 shares of common stock.

***Stock-based Compensation Expense***

The Company accounts for stock-based compensation awards in accordance with ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"). ASC 718 requires all share-based payments to employees, including grants of employee stock options, to be recognized as expense in the consolidated statements of operations based on their grant date fair values. For stock options granted to employees and to members of the Company's board of directors for their services on the board of directors, the Company estimates the grant date fair value of each option award using the Black-Scholes option-pricing model. For stock options subject to service-based vesting conditions, the Company recognizes stock-based compensation expense equal to the grant date fair value of stock options on a straight-line basis over the requisite service period.

Share-based payments issued to non-employees are initially recorded at their fair values, and are revalued at each reporting date and as the equity instruments vest and are recognized as expense over the related service period in accordance with the provisions of ASC Topic 505-50, *Equity-Based Payments to Non-Employees*.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (1) the expected stock price volatility, (2) the calculation of expected term of the award, (3) the risk-free interest rate, and (4) the expected dividend yield. Because there had been no public market for the Company's common stock prior to the IPO, there is a lack of company-specific historical and implied volatility data. Accordingly, the Company bases its estimates of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The Company calculates historical volatility based on a period of time commensurate with the expected term. The Company computes expected volatility based on the historical volatility of a representative group of companies with similar characteristics to the Company, including their stages of product development and focus on the life science industry. The Company uses the simplified method as prescribed by the Securities and Exchange Commission's Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term for options granted to employees as the Company does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. For options granted to non-employees, the Company utilizes the contractual term of the arrangement as the basis for the expected term. The Company determines the risk-free interest rate based on a treasury instrument whose term is consistent with the expected term of the stock options. The Company uses an assumed dividend yield of zero as the Company has never

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paid dividends and does not have current plans to pay any dividends on common stock. If factors change or different assumptions are used, the Company's stock-based compensation expense could be materially different in the future.

### *Determination of Fair Value of Common Stock on Grant Dates prior to our Initial Public Offering*

Prior to the IPO, the Company utilized significant estimates and assumptions in determining the fair value of its common stock. The board of directors determined the estimated fair value of the Company's common stock based on a number of objective and subjective factors, including the lack of an active public market for the Company's common and convertible preferred stock; the prices of shares of the Company's convertible preferred stock that the Company had sold to outside investors in arm's length transactions, and the rights, preferences, and privileges of that convertible preferred stock relative to the Company's common stock; the Company's results of operations and financial condition; the Company's entry into license agreements, pursuant to which the Company obtained rights to important intellectual property; the material risks related to the Company's business; the Company's business strategy; the market performance of publicly traded companies in the life sciences and biotechnology sectors; and the likelihood of achieving a liquidity event for the holders of the Company's common stock, such as an IPO, given prevailing market conditions. The Company utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants, *Audit and Accounting Practice Aid Series: Valuation of Privately Held Company Equity Securities Issued as Compensation* (the "AICPA Practice Aid"), to estimate the fair value of its common stock and in performing retrospective valuation analyses for certain grant dates prior to the IPO. The methodologies included the option pricing method utilizing the back-solve method (a form of the market approach defined in the AICPA Practice Aid) and the probability-weighted expected return method based upon the probability of occurrence of certain future liquidity events such as an initial public offering or sale of the Company. Each valuation methodology included estimates and assumptions that required the Company's judgment. Significant changes to the key assumptions used in the valuations could have resulted in different fair values of the Company's common stock at each valuation date.

### *Income taxes*

Income taxes are recorded in accordance with ASC Topic 740, *Income Taxes* ("ASC 740"), which provides for deferred taxes using an asset and liability approach. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial reporting and the tax reporting basis of assets and liabilities and are measured using the enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. The Company provides a valuation allowance against net deferred tax assets unless, based upon the weight of available evidence, it is more likely than not that the deferred tax assets will be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognized the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances.

### *Other Income (Expense), Net*

Other income (expense), net consists primarily of interest income earned on cash equivalents and government grant income, net of re-measurement losses associated with changes in the fair value of the Company's liability for a warrant to purchase preferred stock. Upon the completion of the IPO, the outstanding warrant to purchase preferred stock converted into a warrant to purchase common stock and the Company reclassified the fair value of the warrant to additional paid-in capital. As a result, there were no further remeasurement gains or losses associated with the warrant after the first quarter of 2016.

Prior to 2016, other income (expense), net included re-measurement gains or losses associated with changes in the fair value of the tranche rights associated with the Series A-1 preferred stock and anti-dilutive protection liability associated with the issuance of common stock to certain licensors. In June 2015, upon the issuance of the final tranche of Series A preferred stock, the tranche right liability was settled and reclassified to Series A preferred stock and the anti-dilutive protection liability was settled and reclassified to additional paid-in-capital. Therefore no further re-measurement gains or losses will be recognized related to the tranche rights or the anti-dilutive protection liability.

### ***Comprehensive Loss***

Comprehensive loss is comprised of net loss and other comprehensive income or loss. Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. There was no difference between net loss and comprehensive loss for each of the periods presented in the accompanying consolidated financial statements.

### ***Concentrations of Credit Risk and Off-Balance Sheet Risk***

The Company has no financial instruments with off-balance sheet risk such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially subject the Company to a concentration of credit risk are cash and cash equivalents and accounts receivable. The Company's cash and cash equivalents are held in accounts at a financial institution that may exceed federally insured limits. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. Accounts receivable primarily consist of amounts due under the collaboration agreement with Juno Therapeutics (Note 8) for which the Company does not obtain collateral. As of December 31, 2016, all of the Company's revenue to date had been generated exclusively from the collaboration with Juno Therapeutics and its award agreement with CFFT.

### ***Segment Information***

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker in deciding how to allocate resources and assess performance. The Company and the Company's chief operating decision maker, the Company's Chief Executive Officer, view the Company's operations and manage the Company's business as a single operating segment, which is the business of developing and commercializing genome editing technology.

### ***Subsequent Events***

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the consolidated financial statements to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure.

### ***Recent Accounting Pronouncements***

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers* ("ASU 2014-09"), which supersedes the revenue recognition requirements in ASC 605, and most industry-specific guidance. The new standard requires that an entity recognize revenue to depict the transfer of 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 update also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. ASU 2014-09 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2017 and should be applied retrospectively to each prior reporting period presented or retrospectively with the cumulative effect of initially applying this update recognized at the date of initial application. Early adoption is permitted beginning after December 15, 2016, including interim reporting periods within those years. In April 2016, the FASB issued ASU No. 2016-10, *Revenue from Contracts with Customers: Identifying Performance Obligations and Licensing* ("ASU 2016-10"), which clarifies certain aspects of identifying performance obligations and licensing implementation guidance. In May 2016, the FASB issued ASU No. 2016-12, *Revenue from Contracts with Customers: Narrow-Scope Improvements and Practical Expedients* ("ASU 2016-12"), related to disclosures of remaining performance obligations, as well as other amendments to guidance on collectability, non-cash consideration and the presentation of sales and other similar taxes collected from customers. These standards have the same effective date and transition date as ASU 2014-09. The Company has two revenue arrangements, its license and collaboration with Juno Therapeutics and its arrangement with CFFT pursuant to which it has recognized a total of \$5.7 million and \$0.3 million, respectively, through December 31, 2016. The Company is analyzing the potential



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impact that ASU 2014-09, ASU 2016-10 and ASU 2016-12 may have on its historical revenue recognition under these two arrangements. This analysis includes, but is not limited to, reviewing variable consideration as it relates to its agreements, reviewing the method and timing of recognition of the license payment, research funding and the \$2.5 million milestone received from Juno Therapeutics, assessing potential disclosures and evaluating the impact of each potential method of adoption on the Company's consolidated financial statements. In addition, the Company continues to monitor additional changes, modifications, clarifications or interpretations undertaken by the FASB, which may impact its conclusions.

In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements - Going Concern: Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern* ("ASU 2014-15"). ASU 2014-15 is intended to define management's responsibility to evaluate whether there is substantial doubt about an organization's ability to continue as a going concern and to provide related footnote disclosures, if required. ASU 2014-15 is effective for annual reporting periods ending after December 15, 2016, and applies to annual and interim periods thereafter. The Company adopted this standard during the three months ended December 31, 2016. The Company completed its evaluation and determined there was not substantial doubt about the organization's ability to continue as a going concern.

In February 2016, the FASB issued ASU No. 2016-02, *Leases* ("ASU 2016-02"), which applies to all leases and will require lessees to record most leases on the balance sheet, but recognize expense in a manner similar to the current standard. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018 and interim periods within those years. Entities are required to use a modified retrospective approach of adoption for leases that exist or are entered into after the beginning of the earliest comparative period in the financial statements. Full retrospective application is prohibited. The Company is evaluating the impact that this ASU may have on its consolidated financial statements.

In March 2016, the FASB issued ASU 2016-09, *Improvements to Employee Share-Based Payment Accounting*, which simplifies share-based payment accounting through a variety of amendments. The standard will be effective for annual reporting periods and interim periods within those annual periods, beginning after December 15, 2016, and early adoption is permitted. The new standard became effective for the Company on January 1, 2017 and is not expected to have a material impact on the consolidated financial statements.

In October 2016, the FASB issued ASU 2016-18, *Restricted Cash* ("ASU 2016-18"), which requires that a statement of cash flows explain the change during the period in the total of cash, cash equivalents, and restricted cash or restricted cash equivalents. Therefore, amounts described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 is effective for fiscal years beginning after December 15, 2017, and interim periods within those years. Early adoption is permitted. The Company is evaluating the potential impact that the adoption of ASU 2016-18 will have on the Company's financial position or results of operations.

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**3. Fair Value Measurements**

Assets measured at fair value on a recurring basis as of December 31, 2016 are as follows (in thousands):

<b>Financial Assets</b>	<b>December 31, 2016</b>	<b>Quoted Prices in Active Markets for Identical Assets (Level 1)</b>	<b>Significant Other Observable Inputs (Level 2)</b>	<b>Significant Unobservable Inputs (Level 3)</b>
Cash and cash equivalents	\$ 185,323	185,323	\$ —	\$ —
Money market funds, included in restricted cash and other non-current assets	1,619	1,619	—	—
<b>Total financial assets</b>	<b>\$ 186,942</b>	<b>\$ 186,942</b>	<b>\$ —</b>	<b>\$ —</b>

Assets and liabilities measured at fair value on a recurring basis as of December 31, 2015 are as follows (in thousands):

<b>Financial Assets</b>	<b>December 31, 2015</b>	<b>Quoted Prices in Active Markets for Identical Assets (Level 1)</b>	<b>Significant Other Observable Inputs (Level 2)</b>	<b>Significant Unobservable Inputs (Level 3)</b>
Cash and cash equivalents	\$ 143,180	\$ 143,180	\$ —	\$ —
Money market funds, included in other current assets	320	320	—	—
<b>Total financial assets</b>	<b>\$ 143,500</b>	<b>\$ 143,500</b>	<b>\$ —</b>	<b>\$ —</b>
<b>Financial Liabilities</b>				
Warrant liability	\$ 289	\$ —	\$ —	\$ 289
<b>Total financial liabilities</b>	<b>\$ 289</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ 289</b>

There were no transfers between fair value measurement levels during the years ended December 31, 2016 or 2015. The fair value of the preferred stock warrant liability was determined based on “Level 3” inputs utilizing the Black-Scholes option pricing model. Upon the completion of the IPO, the Company’s outstanding warrant to purchase preferred stock converted into a warrant to purchase common stock and the Company reclassified the fair value of the warrant to additional paid-in capital.

The following table provides a roll-forward of the fair value of the assets and liabilities measured at fair value on a recurring basis using Level 3 significant unobservable inputs (in thousands):

	<b>Warrant Liability</b>
Balance at December 31, 2015	\$ 289
Changes in fair value, included in other income (expense), net	87
Reclassification to additional paid-in capital in connection with the initial public offering	(376)
Balance at December 31, 2016	<b>\$ —</b>

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#### 4. Prepaid Expenses and Other Current Assets

Prepaid expense and other current assets consisted of the following (in thousands):

	As of December 31,	
	2016	2015
Prepaid expenses	\$ 1,662	\$ 460
Restricted cash	—	320
Other	110	6
Total	<u>\$ 1,772</u>	<u>\$ 786</u>

#### 5. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	As of December 31,	
	2016	2015
Building	\$ 35,941	\$ —
Laboratory equipment	5,130	2,215
Computer equipment	392	447
Furniture and office equipment	170	74
Leasehold improvements	200	23
Software	101	—
Total property and equipment	41,934	2,759
Less: accumulated depreciation	(1,556)	(629)
Property and equipment, net	<u>\$ 40,378</u>	<u>\$ 2,130</u>

The Company recorded \$1.2 million, \$0.5 million, and \$0.2 million in depreciation expense during the years ended December 31, 2016, 2015 and 2014, respectively.

#### 6. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	As of December 31,	
	2016	2015
Patent and license fees	\$ 13,251	\$ 3,395
Deferred initial public offering costs	—	283
Employee compensation costs	2,480	1,016
Professional services	729	382
Research and development	443	—
Other	536	380
Total	<u>\$ 17,439</u>	<u>\$ 5,456</u>

#### 7. Commitments and Contingencies

##### *Facility Leases*

In December 2013, the Company entered into an agreement to sublease its facility under a non-cancelable operating lease that was set to expire at the end of September 2016. The Company extended the sublease through November 1, 2016. Pursuant to the sublease agreement, the Company maintained restricted cash of \$0.3 million in a

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collateral account that was held until the termination of the Company's obligations under the agreement. The sublease agreement could not be extended beyond the expiration date of the sublease. The sublease contained escalating rent clauses which required higher rent payments in future years. The Company expensed rent on a straight-line basis over the term of the sublease, including any rent-free periods. The deposit was recorded in prepaid expenses and other current assets in the accompanying consolidated balance sheet as of December 31, 2015.

In November 2015, the Company entered into a real estate license agreement to sublease from the licensor additional laboratory space in Cambridge, Massachusetts. The term of the lease was from December 1, 2015 to November 30, 2016. The Company's contractual obligation related to lease payments over the term of the sublease was approximately \$1.9 million.

### *Hurley Street, Cambridge, MA*

In February 2016, the Company entered into a lease agreement for approximately 59,783 square feet of office and laboratory space located on Hurley Street in Cambridge, Massachusetts. The term of the lease began on October 1, 2016. In connection with the lease and as a security deposit, the Company deposited with the landlord a letter of credit in the amount of approximately \$1.6 million. Subject to the terms of the lease and certain reduction requirements specified therein, the \$1.6 million security deposit may decrease over time. The letter of credit, which is collateralized by the Company with cash held in a money market account, is recorded in restricted cash and other non-current assets in the accompanying consolidated financial statement as of December 31, 2016.

In connection with this lease, the landlord provided a tenant improvement allowance for costs associated with the design, engineering, and construction of tenant improvements for the leased facility. For accounting purposes, the Company was deemed the owner of the building during the construction period due to the fact that the Company was involved in the construction project, including having responsibilities for cost overruns for planned tenant improvements that did not qualify as "normal tenant improvements" under the lease accounting guidance. Throughout the construction period, the Company recorded the project construction costs incurred as an asset, along with a corresponding facility lease obligation, on its balance sheet for the total amount of the project costs incurred whether funded by the Company or the landlord.

Construction was completed in October 2016, and the Company considered the requirements for sale-leaseback accounting treatment, which included an evaluation of whether all risks of ownership had transferred back to the landlord, as evidenced by a lack of continuing involvement in the leased property. The Company determined that the arrangement did not qualify for sale-leaseback accounting treatment, the building asset would remain on the Company's balance sheet at its historical cost, and such asset would be depreciated over its estimated useful life of 30 years.

The Company bifurcates its future lease payments pursuant to the Hurley Street lease into (i) a portion that is allocated to the building and (ii) a portion that is allocated to the land on which the building is located, which is recorded as rental expense. Although the Company did not begin making lease payments pursuant to the Hurley Street lease until November 2016, the portion of the lease obligation allocated to the land is treated for accounting purposes as an operating lease that commenced upon execution of the Hurley Street lease in February 2016. During the year ended December 31, 2016, the Company recognized \$0.5 million of rental expense attributable to the land.

The lease will continue until October 2023. The Company has the option to extend the lease for an additional five year term at market-based rates. The Company began using this space as its headquarters in October 2016 and rental payments for this property began in November 2016. The base rent is subject to increases over the term of the lease. The non-cancelable minimum annual lease payments, excluding the Company's share of the facility operating expenses and

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other costs that are reimbursable to the landlord under the lease, consist of the following (in thousands):

Year ended December 31,	11 Hurley Street Lease
2017	\$ 3,957
2018	4,055
2019	4,155
2020	4,257
2021	4,362
2022 and thereafter	8,271
Total minimum lease payments	\$ 29,057

Rent expense of approximately \$2.5 million, \$1.0 million, and \$0.9 million was incurred during the years ended December 31, 2016, 2015 and 2014, respectively.

***Licensor Expense Reimbursement***

The Company is obligated to reimburse The Broad Institute Inc. (the "Broad") and the President and Fellows of Harvard College ("Harvard") for expenses incurred by each of them associated with the prosecution and maintenance of the patent rights that the Company licenses from them pursuant to the license agreement by and among the Company, Broad and Harvard, including the interference and opposition proceedings involving patents licensed to the Company under the license agreement. As such, the Company anticipates that it has a substantial commitment in connection with these proceedings until such time as these proceedings have been resolved, but the amount of such commitment is not determinable. The Company incurred an aggregate of \$23.1 million, \$9.4 million and \$1.7 million in expense during the years ended December 31, 2016, 2015 and 2014, respectively, for such reimbursement.

***Success Payments***

In 2016, the Company entered into patent license agreements with The General Hospital Corporation, d/b/a Massachusetts General Hospital ("MGH"), and Broad (collectively, the "2016 License Agreements"). Pursuant to the terms of the 2016 License Agreements, the Company is required to make certain success payments to MGH, Broad, and Wageningen University ("Wageningen" and such payments, collectively, the "Success Payments"), payable in cash or, at the Company's election common stock in the case of MGH or, in the case of Broad and Wageningen, promissory notes payable in cash or, at the Company's election subject to certain conditions, common stock of the Company, into common stock of the Company subject to certain conditions. The Success Payments are payable, if and when, the Company's market capitalization reaches specified thresholds or upon a sale of the Company for consideration in excess of those thresholds, as discussed more fully in Note 8 (collectively, the "Payment Conditions").

The Success Payments were accounted for under the provisions of FASB ASC, Topic 505-50, *Equity-Based Payments to Non-Employees*. The Company has the right to terminate any of the agreements at will upon written notice. Absent any of the Payment Conditions being achieved prior to termination, the Company would not be obligated to pay any Success Payments. As such, the Company will recognize the expense and liability associated with each Success Payment upon achievement of the associated Payment Conditions, if ever. The Company did not incur any expenses related to Success Payments during the year ended December 31, 2016.

***Notes Payable***

In December 2016, in connection with the Company's entry into certain of the 2016 License Agreements with Broad, it issued promissory notes (the "Notes"), in an aggregate principal amount of \$10.0 million to Broad and Wageningen. Principal and interest on the Notes is payable in December 2017, or if earlier, a specified period of time following a company sale event. The Notes bear interest at a rate of 4.8% per annum. The Company may elect to make any payment of amounts outstanding under the Notes either in the form of cash or, subject to certain conditions, in shares of the Company's common stock of equal value, with such shares being valued for such purpose at the closing price of the Company's common stock as reported the NASDAQ Stock Market for the trading day immediately preceding the

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date of such payment if the Company's common stock is then listed on the NASDAQ Stock Market. In the event of a change of control of the Company or a sale of the Company, the Company will be required to pay all remaining principal and accrued interest on the Notes in cash within a specified period following such event. Under the terms of certain of the 2016 License Agreements with Broad, the Company may be required to issue additional promissory notes in connection with potential Success Payments. The Company believes that the carrying value of the Notes approximates their fair value based on Level 3 inputs including a quoted rate.

### ***Litigation***

The Company is not a party to any litigation and did not have contingency reserves established for any litigation liabilities as of December 31, 2016 and 2015.

## **8. Significant Agreements**

### ***Juno Therapeutics Collaboration Agreement***

#### ***Summary of Agreement***

In May 2015, the Company entered into a Collaboration and License Agreement (the "Collaboration Agreement") with Juno Therapeutics. The collaboration is focused on the research and development of engineered T cells with chimeric antigen receptors ("CARs") and T cell receptors ("TCRs") that have been genetically modified to recognize and kill other cells. The parties will pursue the research and development of CAR and TCR engineered T cell products utilizing the Company's genome editing technologies with Juno Therapeutics' CAR and TCR technologies across three research areas.

The collaborative program of research to be undertaken by the parties pursuant to the Collaboration Agreement will be conducted in accordance with a mutually agreed upon research plan which outlines each party's research and development responsibilities across the three research areas. The Company's research and development responsibilities under the research plan are related to generating genome editing reagents that modify gene targets selected by Juno Therapeutics. Juno Therapeutics is responsible for evaluating and selecting for further research and development CAR and TCR engineered T cell products modified with the Company's genome editing reagents. Except with respect to the Company's obligations under the mutually agreed upon research plan, Juno Therapeutics has sole responsibility, at its own cost, for the worldwide research, development, manufacturing and commercialization of products within each of the three research areas for the diagnosis, treatment or prevention of any cancer in humans through the use of engineered T cells, excluding the diagnosis, treatment or prevention of medullary cystic kidney disease 1 (the "Exclusive Field").

The initial term of the research program commenced on May 26, 2015 and continues for five years ending on May 26, 2020 (the "Initial Research Program Term"). Juno Therapeutics may extend the Initial Research Program Term for up to two additional one year periods upon the payment of extension fees for each one year extension period, assuming the Company has agreed to the extension request(s) (together, the initial term and any extension period(s) are referred to as the "Research Program Term").

Under the terms of the Collaboration Agreement, the Company granted to Juno Therapeutics during the Research Program Term a nonexclusive, worldwide, royalty-free, sublicensable (subject to certain conditions) license under certain of the intellectual property controlled by the Company solely for the purpose of conducting activities required under the specified research under the Collaboration Agreement: (i) conduct activities assigned to Juno Therapeutics under the research plan, (ii) conduct activities assigned to the Company under the research plan that the Company fails or refuses to conduct in a timely manner, (iii) use certain genome editing reagents generated under the research program to research, evaluate and conduct preclinical testing and development of certain engineered T cells and (iv) evaluate the data developed in the conduct of activities under the research plan (the "Research License"). Additionally, as it relates to two of the three research areas, the Company granted to Juno Therapeutics an exclusive, milestone and royalty-bearing, sublicensable license under certain of the intellectual property controlled by the Company to research, develop, make and have made, use, offer for sale, sell, import and export selected CAR and TCR engineered T cell products in the Exclusive Field on a worldwide basis, specifically as it relates to certain targets selected by Juno

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Therapeutics pursuant to the research program. Furthermore, as it relates to the same two research areas, the Company granted to Juno Therapeutics a non-exclusive, milestone and royalty-bearing, sub licensable license under certain of the intellectual property controlled by the Company to use genome editing reagents generated under the research program that are used in the creation of certain CAR or TCR engineered T cell products on which Juno Therapeutics has filed an IND in the Exclusive Field for the treatment or prevention of a cancer in humans to research, develop, make and have made, use, offer for sale, sell, import and export those CAR or TCR engineered T cell products in all fields outside of the Exclusive Field (the “Non-Exclusive Field”) on a worldwide basis, specifically as it relates to certain targets selected by Juno Therapeutics pursuant to the research program (together, the license in the Exclusive Field and the license in the Non-Exclusive Field are referred to as the “Development and Commercialization License” for each particular research area). Lastly, as it relates to the third research area, the Company granted to Juno Therapeutics a milestone and royalty-bearing, sublicensable license under certain of the intellectual property controlled by the Company to use the genome editing reagents generated under the research program that are associated with certain CAR or TCR engineered T cell products to research, develop, make and have made, use, offer for sale, sell, import or export those CAR or TCR engineered T cell products in the Exclusive Field on a worldwide basis, specifically as it relates to certain products selected by Juno Therapeutics pursuant to the research program. The license associated with the third research area is exclusive as it relates to CAR or TCR engineered T cell products directed to certain targets as selected by Juno Therapeutics, but is otherwise non-exclusive (the “Development and Commercialization License” for the third research area).

The Collaboration Agreement will be managed on an overall basis by a project leader from each of the Company and Juno Therapeutics. The project leaders will serve as the contact point between the parties with respect to the research program and will be primarily responsible for facilitating the flow of information, interaction, and collaboration between the parties. In addition, the activities under the Collaboration Agreement during the Research Program Term will be governed by a joint research committee (the “JRC”) formed by an equal number of representatives from the Company and Juno Therapeutics. The JRC will oversee, review and recommend direction of the research program. Among other responsibilities, the JRC will monitor and report research progress and ensure open and frequent exchange between the parties regarding research program activities.

Under the terms of the Collaboration Agreement, the Company received a \$25.0 million up-front, non-refundable, non-creditable cash payment. In addition, Juno Therapeutics will pay to the Company an aggregate of up to \$22.0 million in research and development funding over the initial five year term of the research program across the three research areas consisting primarily of funding for up to a specified maximum number of full time equivalents personnel each year over the initial five year term of the research program across three research areas. Under the terms of the Collaboration Agreement, there is no incremental compensation due to the Company with respect to the Development and Commercialization License granted to Juno Therapeutics associated with the first target or product, as applicable, designated by Juno Therapeutics within each of the three research areas. However, for two of the three research areas, Juno Therapeutics has the option to purchase up to three additional Development and Commercialization Licenses associated with other gene targets for an additional fee of approximately \$2.5 million per target. In addition, Juno Therapeutics would be required to make certain milestone payments to the Company upon the achievement of specified development, regulatory and commercial events. More specifically, for the first product to achieve the associated event in each of the three research areas, the Company is eligible to receive up to a \$77.5 million in development milestone payments and up to \$80 million in regulatory milestone payments. In addition, the Company is eligible to receive additional development and regulatory milestone payments for subsequent products developed within each of the three research areas. Moreover, the Company is eligible for up to \$75.0 million in commercial milestone payments associated with aggregate sales of all products within each of the three research areas. Development milestone payments are triggered upon the achievement of certain specified development criteria or upon initiation of a defined phase of clinical research for a product candidate. Regulatory milestone payments are triggered upon approval to market a product candidate by the United States Food and Drug Administration (“FDA”) or other global regulatory authorities. Commercial milestone payments are triggered when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee.

In addition, to the extent any of the product candidates covered by the licenses conveyed to Juno Therapeutics are commercialized, the Company would be entitled to receive tiered royalty payments of low double digits based on a percentage of net sales. Royalty payments are subject to certain reductions, including for any royalty payments required



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to be made by Juno Therapeutics related to a third-party's intellectual property rights, subject to an aggregate minimum floor. Royalties are due on a licensed product-by-licensed product and country-by-country basis from the date of the first commercial sale of each product in a country until the later of: (i) the tenth anniversary of the first commercial sale of such licensed product in such country and (ii) the expiration date in such country of the last to expire valid claim within the licensed intellectual property covering the manufacture, use or sale of such licensed product in such country. In May 2016, the Company achieved a \$2.5 million milestone under the collaboration resulting from technical progress in a research program to create engineered T cells with CARs and TCRs to treat cancer. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, no additional milestone or royalty payments may ever be received from Juno Therapeutics. As of December 31, 2016, the next potential milestone payment that the Company may be entitled to receive under the agreement is a substantive milestone payment of \$2.5 million for the achievement of certain development criteria. The Company would recognize the milestone payment as revenue upon achievement. There are no cancellation, termination or refund provisions in the Collaboration Agreement that contain material financial consequences to the Company.

Unless earlier terminated, the Collaboration Agreement will continue in full force and effect, on a product-by-product and country-by-country basis until the date no further payments are due to the Company from Juno Therapeutics. Either party may terminate the Collaboration Agreement if the other party has materially breached or defaulted in the performance of any of its material obligations and such breach or default continues after the specified cure period. Either party may terminate the Collaboration Agreement in the event of the commencement of any proceeding in or for bankruptcy, insolvency, dissolution or winding up by or against the other party that is not dismissed or otherwise disposed of within a specified time period. Juno Therapeutics may terminate the Collaboration Agreement for convenience upon not less than six months prior written notice to the Company. The Company may terminate the Collaboration Agreement in the event that Juno Therapeutics brings, assumes, or participates in, or knowingly, willfully or recklessly assists in bringing a dispute or challenge against the Company related to its intellectual property.

Termination of the Collaboration Agreement for any reason does not release either party from any liability which, at the time of such termination, has already accrued to the other party or which is attributable to a period prior to such termination nor preclude either party from pursuing any rights and remedies it may have under the agreement or at law or in equity with respect to any breach of the Collaboration Agreement. If Juno Therapeutics terminates the Collaboration Agreement as a result of the Company's uncured material breach or default, then: (i) the licenses and rights conveyed to Juno Therapeutics will continue as set forth in the agreement, (ii) Juno Therapeutics' obligations related to milestones and royalties will continue as set forth in the agreement and (iii) Juno Therapeutics' rights to prosecute, maintain and enforce certain intellectual property rights will continue as set forth in the agreement. If Juno Therapeutics terminates the Collaboration Agreement for convenience or if the Company terminates the Collaboration Agreement as a result of Juno Therapeutics' uncured material breach or default, then the licenses conveyed to Juno Therapeutics will terminate.

### *Accounting Analysis*

The Company evaluated the Collaboration Agreement in accordance with the provisions of ASC, Topic 605-25, *Revenue Recognition—Multiple Element Arrangements*. The Company's arrangement with Juno Therapeutics contains the following deliverables: (i) research and development services during the Initial Research Program Term (the "R&D Services Deliverable"), (ii) the Research License, (iii) the Development and Commercialization Licenses related to each of the three research areas (each, the "Development and Commercialization License Deliverable" for the respective research area), (iv) significant and incremental discount related to the option to purchase up to three additional Development and Commercialization Licenses for two of the research areas (each, the "Discount Deliverable" for the associated option) and (v) JRC services during the Initial Research Program Term (the "JRC Deliverable").

The Company has determined that the options to purchase additional development and commercialization licenses within two of the research program areas related to other gene targets are substantive options. Juno Therapeutics is not contractually obligated to exercise the options. Moreover, as a result of the uncertain outcome of the discovery, research and development activities, there is significant uncertainty as to whether Juno Therapeutics will decide to exercise its option for any additional gene targets within either of the two applicable research areas. Consequently, the Company is at risk with regard to whether Juno Therapeutics will exercise the options. However, the Company has

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determined that the options to purchase additional development and commercialization licenses with respect to other gene targets within the two applicable research program areas are priced at a significant and incremental discount. As a result, the Company has concluded that the discounts to purchase development and commercialization licenses for up to three additional gene targets within both of the research areas represent separate elements in the arrangement at inception. Accordingly, the deliverables identified at inception of the arrangement include six separate deliverables related to the significant and incremental discount inherent in the pricing of the option to purchase up to three additional development and commercialization licenses for two of the research areas included within the research program.

The Company has concluded that the Research License deliverable does not qualify for separation from the R&D Services Deliverable. As it relates to the assessment of standalone value, the Company has determined that Juno Therapeutics cannot fully exploit the value of the Research License deliverable without receipt of the R&D Services Deliverable. This is primarily due to the fact that Juno Therapeutics must rely upon the Company to provide the research and development services included in the research plan because the services incorporate technology that is proprietary to the Company. The services to be provided by the Company involve unique skills and specialized expertise, particularly as it relates to genome editing technology that is not available in the marketplace. Accordingly, Juno Therapeutics must obtain the research and development services from the Company which significantly limits the ability for Juno Therapeutics to utilize the Research License for its intended purpose on a standalone basis. Therefore, the Research License deliverable does not have standalone value from the R&D Services Deliverable. As a result, the Research License deliverable and the R&D Services Deliverable have been combined as a single unit of accounting (the "R&D Services Unit of Accounting"). Conversely, the Company has concluded that each of the other deliverables identified at the inception of the arrangement has standalone value from each of the other elements based on their nature. Factors considered in this determination included, among other things, the capabilities of the collaboration partner, whether any other vendor sells the item separately, whether the value of the deliverable is dependent on the other elements in the arrangement, whether there are other vendors that can provide the items and if the customer could use the item for its intended purpose without the other deliverables in the arrangement. Additionally, the Collaboration Agreement does not include a general right of return. Accordingly, each of the other deliverables included in the Juno Therapeutics arrangement qualifies as a separate unit of accounting.

Therefore, the Company has identified eleven units of accounting in connection with its obligations under the collaboration arrangement with Juno Therapeutics as follows: (i) the R&D Services Unit of Accounting, (ii) three units of accounting related to the Development and Commercialization Licenses for each of the three research areas, (iii) six units of accounting related to each of the Discount Deliverables, and (iv) the JRC Deliverable.

The Company has determined that neither VSOE of selling price nor TPE of selling price is available for any of the units of accounting identified at inception of the arrangement with Juno Therapeutics. Accordingly, the selling price of each unit of accounting was determined based on the Company's BEP. The Company developed the BEP for all of the units of accounting included in the Collaboration Agreement with the objective of determining the price at which it would sell such an item if it were to be sold regularly on a standalone basis. The Company developed the BEP for the R&D Services Unit of Accounting and the JRC Deliverable primarily based on the nature of the services to be performed and estimates of the associated effort and cost of the services, adjusted for a reasonable profit margin that would be expected to be realized under similar contracts. The Company developed the BEP for each of the Development and Commercialization License units of accounting based on the probability-weighted present value of expected future cash flows associated with each license related to each specific research area. In developing such estimate, the Company also considered applicable market conditions and relevant entity-specific factors, including those factors contemplated in negotiating the agreement, probability of success and the time needed to commercialize a product candidate pursuant to the associated license. The Company developed the BEP for each of the Discount Deliverables based on the estimated value of the associated in-the-money options. In developing such estimate, the Company considered the period to exercise the option, an appropriate discount rate and the likelihood that a market participant who was entitled to the discount would exercise the option.

Allocable arrangement consideration at inception is comprised of: (i) the up-front payment of \$25.0 million, (ii) the research support of \$20.0 million and (iii) payments related to specialized materials costs of \$2.0 million. The research support of \$20.0 million and payments related to specialized materials costs of \$2.0 million represent contingent revenue features because the Company's retention of the associated arrangement consideration is dependent upon its

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future performance of research support services and development of specialized materials. The aggregate allocable arrangement consideration of \$47.0 million was allocated among the separate units of accounting using the relative selling price method as follows: (i) R&D Services Unit of Accounting: \$16.7 million, (ii) Development and Commercialization License for the first research area: \$9.3 million, (iii) Development and Commercialization License for the second research area: \$15.4 million, (iv) Development and Commercialization License for the third research area: \$0.2 million, (v) the first Discount Deliverable for the first research area: \$0.7 million, (vi) the second Discount Deliverable for the first research area: \$0.4 million, (vii) the third Discount Deliverable for the first research area: \$0.2 million, (viii) the first Discount Deliverable for the second research area: \$2.0 million, (ix) the second Discount Deliverable for the second research area: \$1.3 million, and (x) the third Discount Deliverable for the second research area: \$0.8 million. No amounts were allocated to the JRC Deliverable because the associated BSP was determined to be de minimis. The amounts allocated to each of the development and commercialization licenses are based on the respective BSP calculations, which reflect the level of risk and expected probability of success inherent in the nature of the associated research area.

The Company will recognize revenue related to amounts allocated to the R&D Services Unit of Accounting as the underlying services are performed. The Company will recognize revenue related to amounts allocated to each of the Development and Commercialization Licenses upon delivery of the associated license, assuming the research services are substantially complete at the time the license is delivered. The rights to be conveyed to Juno Therapeutics pursuant to each of the Development and Commercialization Licenses extend exclusively to an individual target or product, as applicable; therefore, delivery is deemed to occur upon the designation by Juno Therapeutics of the specific target or product, as applicable, whereupon the license becomes effective. The Company will recognize revenue related to amounts allocated to each of the Discount Deliverables upon the earlier of exercise of the associated option or upon lapsing of the underlying right, if the respective option expires unexercised.

The Company has evaluated all of the milestones that may be received in connection with the Juno Therapeutics arrangement. In evaluating if a milestone is substantive, the Company assesses 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(s) 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. All development and regulatory milestones are considered substantive on the basis of the contingent nature of the milestone, specifically reviewing factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the milestone as well as the level of effort and investment required. Accordingly, such amounts will be recognized as revenue in full in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. All commercial milestones will be accounted for in the same manner as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met. The Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

During the year ended December 31, 2016 and 2015, the Company recognized revenue totaling approximately \$5.7 million (\$2.5 million of which related to the first milestone payment) and \$1.6 million, respectively, with respect to the collaboration with Juno Therapeutics. The Company did not recognize any collaboration revenue in the year ended December 31, 2014. The revenue is classified as collaboration and other research and development revenue in the accompanying consolidated statement of operations.

As of December 31, 2016, there was approximately \$26.0 million of deferred revenue related to the Company's collaboration with Juno Therapeutics, which is classified as long-term on the consolidated balance sheet. As of December 31, 2015, there was approximately \$25.3 million of deferred revenue related to the Company's collaboration with Juno Therapeutics, which was classified as long-term in the accompanying consolidated balance sheet.

***Cystic Fibrosis Foundation Therapeutics, Inc. Award Agreement***

In May 2016, the Company entered into an award agreement (the “CF Award Agreement”) with CFFT, pursuant to which the Company received a development award for up to \$5.0 million in funding over the agreement’s three year term (the “Award”). The funding from the Award is supporting the Company’s cystic fibrosis development program and related technology research and development. The Company is required to contribute additional funds to the program in an amount equal to the funds contributed by CFFT under the agreement.

Pursuant to the terms of the CF Award Agreement, the Company is obligated to make royalty payments to CFFT contingent upon commercialization of an editing package, a delivery package, or a combination thereof, for modification of the cystic fibrosis transmembrane conductance regulator gene, the research or development of which was derived in whole or in part from the development program (a “CF Product”), including payments each equal to two times the amount the Company receives under the agreement, following the first commercial sale of a CF Product in the United States and the European Union, respectively. The Company is also obligated to make a payment to CFFT equal to two times the amount the Company receives under the CF Award Agreement, due in the first calendar year in which the aggregate cumulative net sales of a CF Product exceed \$100.0 million. The payments due will not, in the aggregate, exceed ten percent of net sales of a CF Product in a year; the remaining obligation will be carried forward to subsequent year(s) until the payment of any such remaining payment does not, in the aggregate, exceed ten percent of net sales of a CF Product. The Company is also obligated to make payments to CFFT of up to two times the Award amount if the Company transfers, sells or licenses the development program technology, or if the Company enters into a change of control transaction, with such payments to be credited against the payments due upon commercialization. Following the first year anniversary of the effective date of the agreement, either party can terminate the agreement without cause by providing 90 days’ notice. The Company’s payment obligations survive the termination of the CF Award Agreement.

During the year ended December 31, 2016, the Company recognized revenue of \$0.3 million with respect to the Award. The revenue is classified as collaboration and other research and development revenue in the accompanying consolidated statement of operations.

***Adverum Biotechnologies, Inc. Collaboration, Option, and License Agreement***

In August 2016, the Company entered into an agreement with Adverum Biotechnologies, Inc. (“Adverum”) to explore the delivery of genome editing medicines to treat up to five inherited retinal diseases. Under the terms of the agreement, the Company paid an upfront non-refundable fee of \$1.0 million to evaluate Adverum’s next generation adeno-associated viral vectors (“AAVs”) for use in clinical development. The Company will support all preclinical activities related to this agreement, including research and development activities to be performed by Adverum, with \$0.5 million of the upfront fee being creditable against this funding obligation. Accordingly, the Company has deferred and capitalized \$0.5 million of the \$1.0 million upfront fee as an advance payment for future research and development activities which the Company believes will be incurred in the future. The capitalized amount will be expensed as research and development expenses in the Company’s consolidated statements of operations as the related services are performed. The Company expensed the remaining \$0.5 million as research and development expense in the accompanying statement of operations during the year ended December 31, 2016.

Additionally, the Company may pay, at its discretion, an additional fee of \$1.0 million, per exercise, to exercise an option to receive an exclusive license to Adverum’s next generation AAVs for use in an indication chosen under the agreement. Adverum is also entitled to receive development and regulatory milestone payments up to a maximum of a mid-single digit millions of dollars per license based on the achievement of specific events for a product candidate that includes an Adverum vector (an “Adverum Product”) and a low to mid-single digit millions of dollars based on the achievement of specific events for a product candidate that does not include an Adverum vector (a “Non-Adverum Product”). Adverum is also entitled to receive certain commercial milestone payments for Adverum Products up to a maximum amount of a low double digit million dollar amount per product. The Company is also obligated to pay Adverum single digit to low double digit percentage royalties on net sales of Adverum Products and low single digit percentage royalties on sales of Non-Adverum Products sold in applicable territories during the royalty term.

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### **Other Agreements**

#### *Licensing Agreements*

The Company is a party to a number of license agreements under which the Company licenses patents, patent applications and other intellectual property from third parties. The Company anticipates entering into these types of license agreements in the future. The Company believes the following agreements are significant to the business:

#### *Massachusetts General Hospital Agreements*

In August 2014, the Company entered into an agreement to license certain patent rights owned or co-owned by MGH. Consideration for the granting of the license included the payment of an upfront license fee of \$0.1 million, the issuance of 66,848 shares of the Company's common stock, which was based on 0.5% of the Company's outstanding stock on a fully diluted basis, and the right to receive future issuances of shares of common stock to maintain MGH's ownership following the third tranche of the Company's Series A redeemable convertible preferred stock financing (e.g. anti-dilution protection liability), which was settled in June 2015. MGH is entitled to nominal annual license fees and to receive future clinical, regulatory and commercial milestone payments aggregating to a maximum of \$3.7 million and aggregate of \$1.8 million upon the occurrence of certain sales milestones. The Company is also obligated to pay MGH low single digit percentage royalties on net sales of products for the prevention or treatment of human disease, and ranging from low single digit to low double digit percentage royalties on net sales of other products and services made by the Company, its affiliates or its sublicensees. The royalty percentage depends on the product and service, and whether such licensed product or licensed service is covered by a valid claim within the certain patent rights that the Company licenses from MGH.

In August 2016, the Company entered into a license agreement with MGH (the "2016 MGH Agreement") to license certain patent rights owned or co-owned by MGH (the "Additional MGH Patent Rights"). Consideration for granting the license included the payment of an upfront nonrefundable license fee of \$0.8 million, which the Company recorded as research and development expense in the accompanying consolidated statement of operations. Under the 2016 MGH Agreement, MGH is entitled to nominal annual license fees, clinical and regulatory milestone payments totaling less than \$1.0 million in the aggregate per licensed product up to four licensed products or processes to achieve the specified clinical and regulatory milestones, and commercial sales milestone payments totaling up to \$4.9 million in the aggregate, consisting of milestone payments due upon the first commercial sales for up to four licensed products or processes and milestone payments due upon annual net sales of products or processes meeting specified thresholds. The Company is also obligated to pay MGH royalties of less than 1% on net sales of products and processes for the prevention or treatment of human disease, and royalties of a low single-digit percentage on net sales of products and processes for the prevention or treatment of a non-human animal disease, made by the Company, its affiliates, or its sublicensees. The royalty percentages that the Company is obligated to pay are subject to reduction if at the time of sale if the applicable product or process is not covered by a valid claim within the Additional MGH Patent Rights. Under the 2016 MGH Agreement, the Company is obligated to reimburse MGH for all patent costs and future reasonable costs associated with the prosecution, filing, and maintenance of the licensed patents.

MGH is also entitled under the 2016 MGH Agreement to receive payments of up to \$6.0 million in the event the Company's market capitalization reaches specified thresholds exceeding a low ten-digit dollar amount, on or prior to the expiration or termination of the 2016 MGH Agreement (or if earlier, a Company sale) ("MGH Market Cap Success Payments") or a Company sale for consideration in excess of those thresholds ("MGH Company Sale Success Payments"). Additional MGH Market Cap Success Payments become payable, and the amount of potential MGH Company Sale Success Payments would increase further, if the Company's market capitalization reaches additional higher thresholds and the Company has at least one product candidate that is covered by a claim of an Additional MGH Patent Right and that (i) is the subject of a Phase 1 clinical trial of which the Company or an affiliate or sublicensee of the Company is the sponsor, (ii) was the subject of a Phase 1 clinical trial of which the Company or an affiliate or sublicensee of the Company was the sponsor with the Company having determined to conduct a subsequent clinical trial with respect to such product candidate, or (iii) has been approved for sale in either the United States or European Union. MGH Market Cap Success Payments are payable in cash or shares of Company common stock at the Company's discretion, and MGH Company Sale Success Payments are payable solely in cash.

*The Broad Institute Agreements*

In October 2014, the Company entered into an agreement, the Cas9-I License Agreement, with Broad and Harvard to license certain patent rights owned or co-owned by, or among, Broad, Massachusetts Institute of Technology (“MIT”), and Harvard (collectively, the “Institutions”). Consideration for the granting of the license included the payment of an upfront license issuance fee of \$0.2 million and the issuance of 561,531 shares of the Company’s common stock. The Institutions are collectively entitled to receive clinical and regulatory milestone payments totaling up to \$14.8 million in the aggregate per licensed product approved in the United States, European Union, and Japan for the treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. If the Company undergoes a change of control during the term of the license agreement, the clinical and regulatory milestone payments will be increased by a certain percentage in the mid-double digits. The Company is also obligated to make additional payments to the Institutions, collectively, of up to an aggregate of \$54.0 million upon the occurrence of certain sales milestones per licensed product for the treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. The Institutions are collectively entitled to receive clinical and regulatory milestone payments totaling up to \$4.1 million in the aggregate per licensed product approved in the U.S. and at least one jurisdiction outside the U.S. for the treatment of a human disease based on certain criteria. The Company is also obligated to make additional payments to the Institutions, collectively, of up to an aggregate of \$36.0 million upon the occurrence of certain sales milestones per licensed product for the treatment of a rare disease meeting certain criteria. The Institutions are entitled to receive from the Company nominal annual license fees and a mid-single digit percentage royalties on net sales of products for the prevention or treatment of human disease, and ranging from low single digit to high single digit percentage royalties on net sales of other products and services, made by the Company, its affiliates, or its sublicensees. The royalty percentage depends on the product and service, and whether such licensed product or licensed service is covered by a valid claim within the certain patent rights that the Company licenses from the Institutions.

On December 16, 2016, the Company entered into a license agreement (the “Cpfl License Agreement”), with Broad, for specified patent rights (the “Cpfl Patent Rights”) related primarily to Cpfl compositions of matter and their use for gene editing. Concurrently with entering into the Cpfl License Agreement, the Company, Broad, and Harvard amended and restated the Cas9-I License Agreement as described below. On the same day, the Company and Broad entered into a license agreement (the “Cas9-II License Agreement”) for specified patent rights (the “Cas9-II Patent Rights”) related primarily to certain Cas9 compositions of matter and their use for genome editing. The Company will pay an upfront fee in aggregate of \$16.5 million under these agreements, of which \$10.0 million is in the form of notes payable, described further in Note 7. The upfront fee is recorded in research and development expenses for the year ended December 31, 2016.

*Cpfl License Agreement*

Pursuant to the Cpfl License Agreement, Broad, on behalf of itself, Harvard, MIT, Wageningen, and the University of Tokyo (“UTokyo” and, together with Broad, Harvard, MIT, and Wageningen, the “Cpfl Institutions”) granted the Company an exclusive, worldwide, royalty-bearing, sublicensable license to the Cpfl Patent Rights, to make, have made, use, have used, sell, offer for sale, have sold, export and import products in the field of the prevention or treatment of human disease using gene therapy, editing of genetic material, or targeting of genetic material, subject to certain limitations and retained rights (collectively, the “Cpfl Exclusive Field”), as well as a non-exclusive, worldwide, royalty-bearing sublicensable license to the Cpfl Patent Rights for all other purposes, subject to certain limitations and retained rights. The Company is obligated to use commercially reasonable efforts to research, develop, and commercialize products in the Cpfl Exclusive Field. The Company is also required to achieve certain development milestones within specified time periods for products covered by the Cpfl Patent Rights, with Broad having the right to terminate the Cpfl License Agreement if the Company fails to achieve these milestones within the required time periods.

Broad and Wageningen are collectively entitled to receive clinical and regulatory milestone payments totaling up to \$20.0 million in the aggregate per licensed product approved in the United States, European Union, and Japan for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. The Company is also obligated to make additional payments to Broad and Wageningen, collectively, of up



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to an aggregate of \$54.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. Broad and Wageningen are collectively entitled to receive clinical and regulatory milestone payments totaling up to \$6.0 million in the aggregate per licensed product approved in the United States, European Union and Japan for the prevention or treatment of a human disease that afflicts fewer than a specified number of patients in the aggregate in the United States or a specified number of patients per year in the United States (an “Ultra-Orphan Disease”). The Company is also obligated to make additional payments to Broad and Wageningen, collectively, of up to an aggregate of \$36.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or treatment of an Ultra-Orphan Disease.

Broad and Wageningen, collectively, are entitled to receive, on a product-by-product and country-by-country basis, mid single-digit percentage royalty on net sales of licensed products for the prevention or treatment of human disease, and royalties on net sales of other licensed products and licensed services, made by the Company, its affiliates, or its sublicensees. The royalty percentage depends on the product and service, and whether such licensed product or licensed service is covered by a valid claim within the Cpfl Patent Rights. If the Company is legally required to pay royalties to a third party on net sales of the Company’s products because such third party holds patent rights that cover such licensed product, then the Company can credit up to a specified percentage of the amount paid to such third party against the royalties due to Broad and Wageningen in the same period. Such credit may not exceed 50% of the applicable royalties paid by the Company to the applicable third party. The Company’s obligation to pay royalties will expire on a product-by-product and country-by-country basis upon the later of the expiration of the last to expire valid claim of the Cpfl Patent Rights that covers each licensed product or service in each country or the tenth anniversary of the date of the first commercial sale of the licensed product or licensed service. If the Company sublicenses any of the Cpfl Patent Rights to a third party, Broad and Wageningen, collectively, have the right to receive sublicense income, depending on the stage of development of the products or services in question at the time of the sublicense.

Under the Cpfl License Agreement, Broad and Wageningen are also entitled, collectively, to receive success payments in the event the Company’s market capitalization reaches specified thresholds (the “Cpfl Market Cap Success Payments”) or a Company sale for consideration in excess of those thresholds (the “Cpfl Company Sale Success Payments” and, collectively with the Cpfl Market Cap Success Payments, the “Cpfl Success Payments”). The Cpfl Success Payments payable to Broad and Wageningen range from a mid seven digit dollar amount to a mid eight digit dollar amount, and collectively will not exceed, in aggregate, \$125.0 million, which maximum would be payable only if the Company reaches a market capitalization threshold of \$10.0 billion and has at least one product candidate covered by a claim of a patent right licensed to the Company under either the Cpfl License Agreement or the Cas9-I License Agreement that is or was the subject of a clinical trial pursuant to development efforts by the Company or any Company affiliate or sublicensee. The Cpfl Market Cap Success Payments are payable by the Company in cash or in the form of promissory notes on substantially the same terms and conditions as the Notes (Note 7), except that the maturity date of such notes will, subject to certain exceptions, be 150 days following issuance. Following a change in control of the Company, Cpfl Market Cap Success Payments are required to be made in cash. Company Sale Success Payments are payable solely in cash.

Unless terminated earlier, the term of the Cpfl License Agreement will expire on a country-by-country basis, upon the expiration of the last to expire valid claim of the Cpfl Patent Rights in such country. The Company has the right to terminate the Cpfl License Agreement at will upon four months’ written notice to Broad. Either party may terminate the Cpfl License Agreement upon a specified period of notice in the event of the other party’s uncured material breach of a material obligation, such notice period varying depending on the nature of the breach. Broad may terminate the Cpfl License Agreement immediately if the Company challenges the enforceability, validity, or scope of any Patent Right or assist a third party to do so, or in the event of the Company’s bankruptcy or insolvency.

### ***Amendment and Restatement of Existing License Agreement***

On December 16, 2016, the Company amended and restated the Cas9-I License Agreement to exclude additional fields from the scope of the exclusive license previously granted to the Company, to make the exclusive license to three targets become non-exclusive, subject to the limitation that each of Broad and Harvard would only be permitted to grant a license to only on third party at a time with respect to each such target within the field of the

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exclusive license, and to revise certain provisions relating to the rights of Harvard and Broad to grant further licenses under specified circumstances to third parties that wish to develop and commercialize products that target a particular gene and that otherwise would fall within the scope of the exclusive license under this agreement, so that Harvard and Broad together would have rights substantially similar to the equivalent rights possessed by Broad under the Cpfl License Agreement to designate gene targets for which the designating institution, whether alone or together with an affiliate or third party, has an interest in researching and developing products that would otherwise be covered by rights licensed by Harvard and/or Broad to the Company under this agreement, the Cpfl License Agreement or the Cas9-II Agreement.

### *Cas9-II License Agreement*

Pursuant to the Cas9-II License Agreement, Broad, on behalf of itself, MIT, Harvard, and the University of Iowa Research Foundation, granted the Company an exclusive, worldwide, royalty bearing sublicensable license to certain of the Cas9-II Patent Rights as well as a non-exclusive, worldwide, royalty-bearing sublicensable license to all of the Cas9-II Patent Rights, in each case on terms substantially similar to the licenses granted to the Company under Cpfl License Agreement except, among other things, for the following commitment amounts. Under the Cas9-II License Agreement, the Company will pay an upfront license fee in a low seven digits amount as well as an annual license maintenance fee. The Company is obligated to pay clinical and regulatory milestone payments per licensed product approved in the United States, European Union and Japan for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States totaling up to \$3.7 million in the aggregate, and the sales milestone payments for any such licensed product totaling up to \$13.5 million in the aggregate and clinical and regulatory milestone payments totaling up to \$1.1 million in the aggregate per licensed product approved in the United States and the European Union or Japan for the prevention or treatment of a human disease that afflicts fewer than a specified number of patients in the United States, plus sales milestone payments of up to \$9.0 million for any such licensed product. Consistent with the Cpfl License Agreement, the licensors are entitled to royalties on net sales of products for the prevention or treatment of human disease and other products and services made by the Company, its affiliates, or its sublicensees. Royalties due under other license agreements are creditable against these royalties up to a specified amount in the same period. Lastly, Broad is entitled to receive success payments if the Company's market capitalization reaches specified thresholds ascending from a low ten-digit dollar amount to \$9.0 billion or a Company sale. The potential success payments range from a low seven digit dollar amount to a low eight digit dollar amount and will not exceed, in aggregate, \$30.0 million, which maximum would be owed only if the Company reaches a market capitalization threshold of \$9.0 billion and has at least one product candidate covered by a claim of a patent right licensed to the Company under either the Cas9 II License Agreement or the Cas9-I License Agreement that is or was the subject of a clinical trial pursuant to development efforts by the Company or any Company affiliate or sublicensee.

### *Duke University License Agreement*

In October 2014, the Company entered into an exclusive license agreement with Duke University ("Duke") to access intellectual property and technology related to the CRISPR/Cas9 and TALEN genome editing systems. In consideration for the granting of the license, the Company paid Duke an upfront fee of \$0.1 million. Duke is entitled to receive clinical, regulatory, and commercial milestone payments totaling up to \$0.6 million in the aggregate per licensed product. The Company is also obligated to pay to Duke nominal annual license fees and low single digit royalties based on annual net sales of licensed products and licensed services by the Company and its affiliates and sublicensees.

Each of the above license agreements obligates the Company to use commercially reasonable efforts to research, develop, and commercialize products for the prevention or treatment of human disease. The Company is also required to achieve certain development milestones within specific time periods. Each licensor has the right to terminate the license if the Company fails to achieve the development milestones. Each license agreement requires the Company to pay an annual license maintenance fee and reimburse the licensor for expenses associated with the prosecution and maintenance of the licensed patent rights.

The Company recorded the upfront issuance fees and the fair value of the common stock issued to the licensors as research and development expense (as the licenses do not have alternative future use) in accordance with ASC Topic 730, *Research and Development*. The anti-dilutive protection obligation was classified as a liability and was recorded at



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its grant date fair value on the effective date of the respective agreements with the initial fair value being recorded to research and development expense as it represented additional consideration paid to the licensor in connection with the license agreement. The anti-dilution liability was settled in June 2015.

### **9. Preferred Stock**

#### *Redeemable Convertible Preferred Stock*

In November 2013, the Company entered into a preferred stock purchase agreement (the “Preferred Stock Agreement”) in which it agreed to sell, and the purchasers agreed to purchase up to \$43 million of Series A-1 redeemable convertible preferred stock (“Series A-1 Preferred Stock”) and Series A-2 redeemable convertible preferred stock (“Series A-2 Preferred Stock”) which together with the Series A-1 Preferred Stock is collectively referred to as “Series A Preferred Stock”) in three anticipated tranches. In November 2013, the Company sold 3,260,000 shares of Series A-1 Preferred Stock in exchange for gross cash proceeds of \$3.3 million. The Company issued 2,000,000 shares of Series A-1 Preferred Stock in exchange for cash proceeds of \$2.0 million, 2,500,000 shares of Series A-1 Preferred Stock in exchange for cash proceeds of \$2.5 million, and 500,000 shares of Series A-1 Preferred Stock in exchange for cash proceeds of \$500,000 in interim closings in May 2014, July 2014, and October 2014, respectively. In November 2014, the Company issued 13,000,000 shares of Series A-1 Preferred Stock in exchange for cash proceeds of \$13.0 million. Finally, the Company issued 16,698,672 shares of Series A-2 Convertible Preferred Stock in exchange for cash proceeds of \$21.7 million in June 2015. An executive of the Company purchased 192,027 shares of Series A-2 Preferred Stock for \$0.3 million.

In August 2015, the Company sold 26,666,660 shares of Series B redeemable convertible preferred stock (“Series B Preferred Stock”) for cash proceeds of \$120.0 million.

Prior to the IPO, the holders of the Company's convertible Preferred Stock had certain voting, dividend rights, as well as liquidation preferences and conversion privileges. All rights, preferences, and privileges associated with the convertible Preferred Stock were terminated at the time of the Company's IPO in conjunction with the conversion of all outstanding shares of convertible Preferred Stock into shares of Common Stock.

Upon the closing of the Company's IPO, all outstanding shares of the Company's Preferred Stock were automatically converted into 24,929,709 shares of Common Stock.

#### *Tranche Rights Issued with Series A Preferred Stock*

Included in the terms of the Preferred Stock Agreement were certain rights (“Tranche Rights”) granted to the purchasers of Series A-1 Preferred Stock to purchase and the Company to sell additional shares of Series A-1 and Series A-2 Preferred Stock upon the achievement of performance milestones. The Company concluded the Tranche Rights met the definition of a freestanding financial instrument, as the Tranche Rights were legally detachable and separately exercisable from the Series A-1 Preferred Stock. As the Series A Preferred Stock was redeemable at the election of holders of the then-outstanding shares of Series A Preferred Stock, the Tranche Rights were classified as an asset or liability under ASC Topic 480, *Distinguishing Liabilities from Equity*, and were initially recorded at fair value. The Tranche Rights were then remeasured at fair value at each subsequent reporting period. The fair value of the portion of the Tranche Right, based on the implied value of the Preferred Stock from the Company's third party valuation that was settled at each closing was reclassified to Series A-1 Preferred Stock. The Company recognized other expense of \$35.5 million and \$1.0 million related to the mark to market of Tranche Rights during the year ended December 31, 2015 and 2014, respectively.

#### *Preferred Stock*

On February 8, 2016, the Company filed a restated certificate of incorporation with the Secretary of State of the State of Delaware. The restated certificate amended and restated the Company's certificate of incorporation in its entirety to, among other things increase the authorized number of shares of common stock to 195,000,000 shares, eliminate all

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references to the previously existing series of preferred stock, and authorize 5,000,000 shares of undesignated preferred stock that may be issued from time to time by the Company's board of directors in one or more series. As of December 31, 2016, the Company had no shares of preferred stock issued or outstanding.

## 10. Common Stock

The voting, dividend, and liquidation rights of the holders of the common stock are subject to and qualified by the rights, powers, and preferences of holders of the preferred stock that may be issued from time to time. The common stock had the following characteristics as of December 31, 2016:

### *Voting*

The holders of shares of common stock are entitled to one vote for each share of common stock held at any meeting of stockholders and at the time of any written action in lieu of a meeting.

### *Dividends*

The holders of shares of common stock are entitled to receive dividends, if and when declared by the Company's board of directors. Cash dividends may not be declared or paid to holders of shares of common stock until all unpaid dividends on the redeemable convertible preferred stock have been paid in accordance with their terms. No dividends have been declared or paid by the Company since its inception.

### *Shares Reserved for Future Issuance*

	As of December 31,	
	2016	2015
Shares reserved for redeemable convertible preferred stock outstanding	—	24,929,709
Shares reserved for future issuances of redeemable convertible preferred stock warrants	—	23,076
Shares reserved for outstanding stock option awards under the 2013 Stock Incentive Plan, as amended	1,595,082	1,674,047
Remaining shares reserved, but unissued, for future awards under the 2013 Stock Incentive Plan, as amended	—	2,848,630
Shares reserved for outstanding stock option awards under the 2015 Stock Incentive Plan	1,569,746	—
Remaining shares reserved, but unissued, for future awards under the 2015 Stock Incentive Plan	2,760,472	—
Remaining shares reserved, but unissued, for future awards under the 2015 Employee Stock Purchase Plan	384,615	—
	<u>6,309,915</u>	<u>29,475,462</u>

## 11. Stock-Based Compensation

### *2013 Stock Incentive Plan*

In September 2013, the board of directors adopted the 2013 Stock Incentive Plan, as amended (the "2013 Plan"), which provides for the grant of incentive stock options and nonqualified stock options or other awards including restricted stock awards, unrestricted stock awards, and restricted stock units to the Company's employees, officers, directors, advisors, and consultants for the purchase of up to 1,057,692 shares of the Company's common stock. In June 2014, the 2013 Plan was amended to increase the number of shares reserved thereunder by 1,365,384 shares. In April 2015, the 2013 Plan was amended to increase the number of shares reserved thereunder by 153,846 shares. In July 2015, the 2013 Plan was amended to increase the number of shares reserved thereunder by 3,740,847 shares.

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The terms of stock awards agreements, including vesting requirements, are determined by the board of directors and are subject to the provisions of the 2013 Plan. The stock options granted to employees generally vest over a four-year period and expire ten years from the date of grant. Certain awards contain performance based vesting criteria. There has only been one such award to date. Certain options provide for accelerated vesting in the event of a change in control, as defined. Awards granted to non-employee consultants generally vest monthly over a period of one to four years. In connection with the Company's IPO, the Company's board of directors determined to grant no further awards under the 2013 Plan. As of December 31, 2016, there were 1,595,082 shares reserved for issuance upon the exercise of awards outstanding under the 2013 Plan.

### ***2015 Stock Incentive Plan***

The Company's board of directors adopted and the Company's stockholders approved the 2015 stock incentive plan (the "2015 Plan"), which became effective immediately prior to the effectiveness of the registration statement related to the Company's IPO. The 2015 Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards. As of December 31, 2016, there were 1,569,746 shares reserved for issuance upon the exercise of awards outstanding under the 2015 Plan, and an additional 2,760,472 shares reserved for future awards. The Company's employees, officers, directors and consultants and advisors are eligible to receive awards under the 2015 Plan.

The number of shares reserved for issuance under the 2015 Plan is subject to further increases for (a) any additional shares of the Company's common stock subject to outstanding awards under the 2013 Plan that expire, terminate, or are otherwise surrendered, cancelled, forfeited, or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right and (b) annual increases, to be added as of the first day of each fiscal year, from January 1, 2017 until, and including, January 1, 2026, equal to the lowest of 2,923,076 shares of common stock, 4% of the number of shares of common stock outstanding on such first day of the fiscal year in question and an amount determined by the Company's board of directors.

### ***2015 Employee Stock Purchase Plan***

The Company's board of directors adopted and the Company's stockholders approved the 2015 employee stock purchase plan (the "2015 ESPP"), which became effective upon the closing of the Company's IPO. As of December 31, 2016, there were 384,615 shares reserved for issuance under the 2015 ESPP.

The number of shares reserved for issuance under the 2015 ESPP is subject to annual increases, to be added as of the first day of each fiscal year, from January 1, 2017 until, and including, January 1, 2026, in an amount equal to the least of (a) 769,230 shares of common stock, (b) 1% of the total number of shares of common stock outstanding on the first day of the applicable year, and (c) an amount determined by the board of directors. The Company has not issued any shares under the 2015 ESPP as of December 31, 2016.

### ***Founder Awards***

In September 2013, the Company issued 2,403,845 shares of restricted stock to its non-employee founders for services rendered. The shares vested 25% upon the first issuance of shares of Series A Preferred Stock and then 1.5625% a month through the fourth anniversary of the vesting commencement date. These shares of restricted stock are subject to repurchase rights. Accordingly, the Company has recorded the proceeds from the issuance of restricted stock as a liability in its consolidated balance sheets. The restricted stock liability is reclassified into stockholders' equity (deficit) as the restricted stock vests. In the event that a founder is no longer in the Company's service (whether as a consultant, employee, director, or advisor) prior to the fourth anniversary of the vesting commencement date, the Company has the right to repurchase the unvested shares at \$0.0003 per share. In June 2014, one founder ceased to be in the Company's service and the Company repurchased 285,457 shares of unvested restricted stock from the founder for \$74. Upon a change in control, all unvested founder shares will be released from the Company's repurchase options.

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Stock-based compensation expense associated with these awards is recognized as the awards vest. Unvested awards are remeasured at each reporting period end to reflect the current fair value of such awards on a straight-line basis.

**Stock-Based Compensation Expense**

Total compensation cost recognized for all stock-based compensation awards in the consolidated statements of operations and comprehensive loss was as follows (in thousands):

	2016	Year Ended December 31, 2015	2014
Research and development	\$ 4,234	\$ 3,015	\$ 55
General and administrative	12,647	498	—
Total stock-compensation expense	\$ 16,881	\$ 3,513	\$ 55

**Restricted Stock**

From time to time, upon approval by the board of directors, certain employees and advisors have been granted restricted shares of common stock. These shares of restricted stock are subject to repurchase rights. Accordingly, the Company has recorded the proceeds from the issuance of restricted stock as a liability in the consolidated balance sheets included as a component of other long term liabilities based on the scheduled vesting dates. The restricted stock liability is reclassified into stockholders' equity (deficit) as the restricted stock vests. A summary of the status of and changes in unvested restricted stock as of December 31, 2015 and 2016 is as follows:

	Shares	Weighted Average Grant Date Fair Value Per Share
<b>Unvested Restricted Common Stock as of December 31, 2015</b>	1,596,853	\$ 0.0188
Issued	—	—
Vested	(774,215)	\$ 0.0162
<b>Unvested Restricted Common Stock as of December 31, 2016</b>	822,638	\$ 0.0213

The expense related to restricted stock awards granted to employees and non-employees was \$0 and \$8.3 million, respectively, for the year ended December 31, 2016. The expense related to restricted stock awards granted to employees and non-employees was \$0 and \$2.3 million, respectively, for the year ended December 31, 2015.

As of December 31, 2016, the Company had no unrecognized stock-based compensation expense related to its employee unvested restricted stock awards. As of December 31, 2016, the Company had unrecognized stock-based compensation expense related to its non-employee unvested restricted stock awards of \$3.4 million which is expected to be recognized over a remaining weighted average vesting period of 0.6 years.

**Stock Options**

Certain of the Company's stock option agreements allow for the exercise of unvested awards. During 2014, options to purchase 75,304 shares of common stock for \$0.03 per share were exercised prior to their vesting. The unvested shares are subject to repurchase by the Company if the employees cease to provide service to the Company, with or without cause. As such, the Company does not treat the exercise of unvested options as a substantive exercise. The Company has recorded the proceeds from the exercise of unvested stock options as a liability in the consolidated balance sheets as a component of other long term liabilities based on the scheduled vesting dates. The liability for unvested common stock subject to repurchase is reclassified into stockholders' equity (deficit) as the shares vest.

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The following is a summary of stock option activity for the year ended December 31, 2016:

	Shares	Weighted Average Exercise Price	Remaining Contractual Life	Aggregate Intrinsic Value (in thousands)
<b>Outstanding at December 31, 2015</b>	1,713,385	\$ 6.31	9.6	\$ 15,580
Granted	1,794,746	\$ 20.24	—	—
Exercised	(76,298)	\$ 3.04	—	—
Cancelled	(20,050)	\$ 6.74	—	—
<b>Outstanding at December 31, 2016</b>	<b>3,411,783</b>	<b>\$ 13.71</b>	<b>8.8</b>	<b>\$ 16,190</b>
Vested and expected to vest at December 31, 2016	3,356,306	\$ 13.71	8.8	\$ 15,926
Exercisable at December 31, 2016	568,617	\$ 6.86	8.6	\$ 5,330

The table above reflects unvested stock options as exercised on the dates that the shares are no longer subject to repurchase. The Company had 21,955 and 39,338 shares of unvested common stock at December 31, 2016 and 2015 related to the exercise of unvested stock options.

The total intrinsic value of options exercised for the years ended December 31, 2016, 2015, and 2014 was \$0.9 million, \$0.1 million, and \$0.0, respectively. The total fair value of employee options vested from the years ended December 31, 2016, 2015, and 2014 was \$2.8 million, \$8 thousand, and \$0.0 million, respectively.

Using the Black-Scholes option pricing model, the weighted average fair value of options granted to employees and directors during the years ended December 31, 2016, 2015 and 2014 was \$14.10, \$5.91, and \$0.03, respectively. The expense related to options granted to employees was \$6.0 million, \$0.7 million and \$0.0 million for the years ended December 31, 2016, 2015 and 2014, respectively. There were no stock options granted during the period from September 3, 2013 to December 31, 2013.

The fair value of each option issued to employees and directors was estimated at the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year Ended December 31,		
	2016	2015	2014
Expected volatility	78.4 %	78.8 %	87.6 %
Expected term (in years)	6.25	6.25	6.25
Risk free interest rate	1.5 %	1.7 %	1.9 %
Expected dividend yield	—	—	—

There were 100,000 options granted to persons other than employees and directors during the year ended December 31, 2016. For the year ended December 31, 2016, 2015 and 2014, the fair value of each option issued to persons other than employees and directors was estimated at the date of grant using the Black-Scholes option pricing model with the weighted-average assumptions set forth in the table below:

	Year Ended December 31,		
	2016	2015	2014
Expected volatility	76.5 %	80.0 %	80.5 %
Expected term (in years)	10.0	10.0	9.5
Risk free interest rate	1.6 %	2.2 %	1.5 %
Expected dividend yield	—	—	—

As of December 31, 2016, the Company had unrecognized stock-based compensation expense related to its employee stock options of \$24.5 million which the Company expects to recognize over a remaining weighted average vesting period of 3.0 years.

[Table of Contents](#)**12. 401(k) Savings Plan**

The Company has a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code (the “401(k) Plan”). The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pretax basis. Effective in 2017, the Company will provide a 200% match of employee contributions up to a limit on the Company’s contributions of the lesser of \$6,000 and 3% of the employee’s salary. The Company did not make any contributions to the 401(k) Plan through December 31, 2016.

**13. Income Taxes**

A reconciliation of the income tax expense computed using the federal statutory income tax rate to the Company’s effective income tax rate is as follows:

	Year Ended December 31,	
	2016	2015
Income tax computed at federal statutory tax rate	34.0 %	34.0 %
State taxes, net of federal benefit	3.5 %	2.5 %
General business credit carryovers	1.5 %	0.8 %
Non-deductible expenses	(3.6)%	(17.9)%
Change in valuation allowance	(35.4)%	(19.4)%
	<u>— %</u>	<u>— %</u>

The principal components of the Company’s deferred tax assets and liabilities consist of the following at December 31, 2016 and 2015 (in thousands):

	Year Ended December 31,	
	2016	2015
Deferred tax assets:		
Net operating loss carryforwards	\$ 16,490	\$ 11,466
Tax credit carryforwards	2,014	730
Accrued expenses	7,353	1,652
Capitalized patent costs	16,025	5,985
Deferred revenue	9,672	—
Construction financing lease obligation	13,685	—
Other	2,979	242
Total deferred tax assets	68,218	20,075
Less valuation allowance	(54,300)	(19,938)
Net deferred tax assets	13,918	137
Deferred tax liabilities—depreciation and amortization	(13,918)	(137)
Net deferred taxes	<u>\$ —</u>	<u>\$ —</u>

The Company has incurred net operating losses (“NOL”) since inception. At December 31, 2016 and 2015, the Company had federal and state net operating loss carryforwards of \$82.4 million (which include \$0.7 million of NOL carryforwards from stock-based compensation) and \$58.3 million (which include \$0.1 million of NOL carryforwards from stock-based compensation), respectively, which expire beginning in 2033 and will continue to expire through 2036. As of December 31, 2016 and 2015, the Company had federal and state research and development tax credits carryforwards of \$2.3 million and \$0.8 million, respectively, which expire beginning in 2028 and will continue to expire through 2036. The Company has generated NOL carryforwards from stock-based compensation deductions in excess of expenses recognized for financial reporting purposes (“excess tax benefits”). Excess tax benefits are realized when they

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reduce taxes payable, as determined using a “with and without” method, and are credited to additional paid-in capital rather than as a reduction of the income tax provision.

Under the provisions of the Internal Revenue Code of 1986, as amended (the “Code”), the NOL and tax credit carryforward are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three year period in excess of 50%, as defined under Sections 382 and 383 of the Code, respectively, as well as other similar state provisions. The Company has not performed a full comprehensive Section 382 study to determine any potential loss limitation in the United States or a Section 383 study to determine the appropriate amount of NOL and tax credit carryforwards.

Management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which principally comprise of NOL carryforwards and research and development credit carryforwards. Management has determined that it is more likely than not that the Company will not recognize the benefits of its federal and state deferred tax assets, and as a result, a valuation allowance of \$54.3 million and \$19.9 million has been established at December 31, 2016 and 2015, respectively. The change in the valuation allowance of \$34.4 million for the year ended December 31, 2016 was primary due to additional operating losses, capitalized patent costs and deferred revenue.

The Company applies ASC 740 related to accounting for uncertainty in income taxes. The Company’s reserves related to income taxes are based on a determination of whether, and how much of, a tax benefit take by the Company in its tax filings or positions is more likely than not to be realized following resolution of any potential contingencies present related to the tax benefit. At December 31, 2016 and 2015, the Company had no unrecognized tax benefits. Interest and penalty charges, if any, related to unrecognized tax benefits would be classified as income tax expense in the accompanying statements of operations.

The Company has not as yet conducted a study of its research and development credit carry forwards. This study may result in an adjustment to the Company’s research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company’s research and development credits, and if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated balance sheets or statements of operations if an adjustment were required.

The Company files income tax returns in the U.S. federal tax jurisdiction, the Massachusetts state jurisdiction and the California state jurisdiction. Since the Company is in a loss carryforward position, the Company is generally subject to examination by the U.S. federal, state and local income tax authorities for all tax years in which a loss carryforward is available. The Company did not have any international operations as of December 31, 2016. There are no federal or state audits in process.

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#### 14. Net Loss Per Share

Basic net loss per common share is calculated by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding during the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted average number of common shares and potentially dilutive securities outstanding for the period determined using the treasury stock and if converted methods. Contingently issuable shares are included in the calculation of basic loss per share as of the beginning of the period in which all the necessary conditions have been satisfied. Contingently issuable shares are included in diluted loss per share based on the number of shares, if any, that would be issuable under the terms of the arrangement if the end of the reporting period was the end of the contingency period, if the results are dilutive.

For purposes of the diluted net loss per share calculation, stock options and warrants are considered to be common stock equivalents, but they were excluded from the Company's calculation of diluted net loss per share allocable to common stockholders because their inclusion would have been anti-dilutive. Therefore, basic and diluted net loss per share applicable to common stockholders was the same for all periods presented. Contingently issuable shares of common stock pursuant to the 2016 License Agreements and Notes (Note 7) are excluded from the calculation of basic and diluted net loss per share calculation as the Payment Conditions have not been satisfied.

Upon the closing of the IPO in February 2016, the Company sold 6,785,000 shares of common stock and issued an additional 24,929,709 shares of common stock in connection with the automatic conversion of its redeemable convertible preferred stock. The issuance of these shares resulted in a significant increase in the Company's weighted-average shares outstanding for the fiscal year ended December 31, 2016 when compared to the prior year and is expected to continue to impact the year-over-year comparability of the Company's net loss per share calculations for the next three months.

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

	As of December 31,	
	2016	2015
Redeemable convertible preferred stock	—	24,929,709
Warrant to purchase redeemable convertible preferred stock	—	23,076
Unvested restricted common stock	822,638	1,596,853
Outstanding stock options	3,411,783	1,713,385
Total	<u>4,234,421</u>	<u>28,263,023</u>

#### 15. Related-Party Transactions

During the year ended December 31, 2016 and 2015, the Company paid a related party \$1.4 million and \$1.2 million in rent and facility-related fees, respectively. In addition, during the year ended December 31, 2015 and 2014, the Company paid one of its investors \$0.1 million and \$0.2 million in professional fees, respectively.



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The following table contains selected quarterly financial information from 2016 and 2015. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	Three months ended			
	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
	(in thousands, except per share data)			
Total revenue	\$ 805	\$ 3,388	\$ 962	\$ 898
Total operating expenses	18,644	22,588	22,127	39,882
Total other expense, net	94	158	145	(392)
Net loss	<u>\$ (17,745)</u>	<u>\$ (19,042)</u>	<u>\$ (21,020)</u>	<u>\$ (39,376)</u>
Net loss applicable to common stockholders	<u>\$ (17,792)</u>	<u>\$ (19,042)</u>	<u>\$ (21,020)</u>	<u>\$ (39,376)</u>
Net loss per share applicable to common stockholders — basic and diluted	<u>\$ (0.80)</u>	<u>\$ (0.54)</u>	<u>\$ (0.59)</u>	<u>\$ (1.10)</u>

	Three months ended			
	March 31, 2015	June 30, 2015	September 30, 2015	December 31, 2015
	(in thousands, except per share data)			
Total revenue	\$ —	\$ 167	\$ 670	\$ 792
Total operating expenses	5,161	10,563	8,052	13,165
Total other expense, net	(130)	(37,175)	(23)	(260)
Net loss	<u>\$ (5,291)</u>	<u>\$ (47,571)</u>	<u>\$ (7,405)</u>	<u>\$ (12,633)</u>
Net loss applicable to common stockholders	<u>\$ (5,386)</u>	<u>\$ (47,667)</u>	<u>\$ (7,509)</u>	<u>\$ (12,732)</u>
Net loss per share applicable to common stockholders — basic and diluted	<u>\$ (2.75)</u>	<u>\$ (21.45)</u>	<u>\$ (2.57)</u>	<u>\$ (4.05)</u>

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

None.

**Item 9A. Controls and Procedures.**

**Evaluation of Disclosure Controls and Procedures**

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2016. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2016, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

**Management’s Report on Internal Control over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with general accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the 2013 framework in Internal Control –Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under that framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2016.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for "emerging growth companies".

**Changes in Internal Control over Financial Reporting**

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during our fiscal quarter ended December 31, 2016 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

**Item 9B. Other Information.**

None.

**PART III****Item 10. Directors, Executive Officers and Corporate Governance.****Executive Officers and Directors**

The following table sets forth the name, age, and position of each of our executive officers and directors as of February 15, 2017.

Name	Age	Position
<b>Executive Officers</b>		
Katrine S. Bosley	48	President and Chief Executive Officer, Director
Charles Albright, Ph.D.	59	Chief Scientific Officer
Gerald Cox, M.D., Ph.D.	58	Chief Medical Officer
Andrew A. F. Hack, M.D., Ph.D.	43	Chief Financial Officer
Alexandra Glucksmann, Ph.D.	58	Chief Operating Officer
<b>Non-Employee Directors</b>		
Kevin Bitterman, Ph.D.	40	Director
Alexis Borisy <sup>(1)</sup>	45	Director
Douglas G. Cole, M.D. <sup>(1)(2)(3)</sup>	56	Director
John D. Mendlein, Ph.D., J.D. <sup>(2)(3)</sup>	57	Director
Boris Nikolic, M.D. <sup>(1)(3)</sup>	46	Director
Akshay K. Vaishnav, M.D., Ph.D. <sup>(2)</sup>	54	Director

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

**Executive Officers**

**Katrine S. Bosley** has served as our President and Chief Executive Officer and a member of our board of directors since June 2014. Prior to joining Editas, Ms. Bosley was the Entrepreneur-in-Residence at The Broad Institute from September 2013 to May 2014. She served as Chief Executive Officer of Avila Therapeutics Inc., or Avila, a biotechnology company, from May 2009 to March 2012, when Avila was acquired by Celgene Corporation, or Celgene, a public biopharmaceutical company. Ms. Bosley served as President, Celgene Avilomics Research at Celgene from March 2012 to May 2012. Before Avila, she was Vice President, Strategic Operations at Adnexus, a Bristol-Myers Squibb Company and was Vice President, Business Development at Adnexus Therapeutics Inc., or Adnexus, a biotechnology company, before that. She joined Adnexus from Biogen Idec, Inc., a public biotechnology company, where she held roles in business development, commercial operations, and portfolio strategy in the United States and Europe. Earlier, she was part of the healthcare team at the venture firm Highland Capital Partners. Ms. Bosley currently serves as chairman of the board of directors of Genocera Biosciences, Inc., a public biotechnology company, and is a director of Galapagos NV, a public biotechnology company. She also serves on the board of directors of the Biotechnology Industry Organization, a not-for-profit organization. Ms. Bosley graduated from Cornell University with a B.A. in biological sciences. We believe that Ms. Bosley's operational and historical experience with Editas gained from serving as our President and Chief Executive Officer and member of our board of directors, combined with her prior experiences in creating strategic and business development value and her network in the biopharmaceutical industry, qualifies her to serve as a member of our board of directors.

**Charles Albright Ph.D.**, has served as our Chief Scientific Officer since August 2016. Prior to joining Editas, Albright served in a variety of roles at Bristol-Myers Squibb Company, a biopharmaceutical company, from January

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2004 to August 2016, serving most recently as the Vice President, Genetically Defined Diseases and Genomics. Dr. Albright received his B.S. in chemical engineering and a Ph.D. in biology from the Massachusetts Institute of Technology.

**Gerald Cox, M.D., Ph.D.**, has served as our Chief Medical Officer since October 2016. Prior to joining Editas, Dr. Cox served in a variety of roles at Sanofi Genzyme, a biotechnology company, from August 2000 to August 2016, serving most recently as the Vice President of Clinical Development for Rare Diseases. Since July 1994, Dr. Cox has served as a Staff Physician in Genetics at Boston Children's Hospital and, since August 1994, as an Instructor in Pediatrics at Harvard Medical School. Dr. Cox received his B.A. in biology from Harvard College and his M.D. and Ph.D. from the University of California at San Diego.

**Andrew A. F. Hack, M.D., Ph.D.**, has served as our Chief Financial Officer since July 2015. Prior to joining Editas, from May 2011 to June 2015, Dr. Hack was a portfolio manager at Millennium Management LLC, an institutional asset manager, where he ran a healthcare fund focused on biotechnology, pharmaceutical, and medical device companies. Before joining Millennium Management, Dr. Hack was a healthcare analyst at HealthCor Management, L.P., a registered investment advisor, from December 2008 to May 2011. Prior to HealthCor, Dr. Hack served as a healthcare analyst for hedge fund Carlyle-Blue Wave Partners and as principal of the MPM BioEquities Fund, a hedge fund that was affiliated with MPM Capital. Dr. Hack began his investment career covering the biotechnology sector at investment banks Banc of America Securities LLC and Rodman & Renshaw, LLC. Dr. Hack co-founded Reify Corporation, a life science tools and drug discovery company. Dr. Hack serves as a director of Mersana Therapeutics, Inc., a private company. Dr. Hack received his B.A. in biology with special honors from the University of Chicago, where he also received his M.D. and Ph.D.

**Alexandra Glucksmann, Ph.D.**, has served as our Chief Operating Officer since April 2015. From November 2013 to April 2015, she served as our interim Chief Operating Officer. Prior to joining Editas, she served as Senior Vice President of Research and Business Operations at Cerulean Pharma Inc., then a private pharmaceutical company, from 2006 until June 2013. Prior to joining Cerulean, Dr. Glucksmann spent 13 years at Millennium Pharmaceuticals, Inc., a pharmaceutical company, where she held a series of positions. She is the chairperson of the board of directors of Women Entrepreneurs in Science and Technology. Dr. Glucksmann was a post-doctoral fellow at the Massachusetts Institute of Technology and holds a Ph.D. with honors from the University of Chicago and a B.S. in molecular biology from the University of Wisconsin.

### **Non-Employee Directors**

**Kevin Bitterman, Ph.D.**, has served as a member of our board of directors since June 2014. From November 2013 until June 2014, Dr. Bitterman served as our President. Dr. Bitterman currently serves as a partner at venture firm Polaris Partners, or Polaris, where he has been employed since 2004 and where he focuses on investments in life sciences companies. Dr. Bitterman is a cofounder of Sirtris Pharmaceuticals, Inc., which was acquired by GlaxoSmithKline plc., and was the founding CEO at Visterra Inc. and Morpnic Rock, LLC. Dr. Bitterman serves as a director of Genocoea Biosciences, Inc., a public biopharmaceutical company, and of Direct Vet Marketing, Inc., Epacing Inc., Kala Pharmaceuticals, Inc., KSQ Therapeutic, LLC, Morpnic Rock Therapeutic LLC, Neuronetics, Inc., and TARIS Biomedical, Inc., each a private company. Dr. Bitterman received a Ph.D. in genetics from Harvard Medical School and a B.A. in biological sciences from Rutgers College. We believe that Dr. Bitterman's extensive experience investing in, guiding, and leading start-up and early phase companies, as well as his experience as a director of other companies, qualifies him to serve as a member of our board of directors.

**Alexis Borisy** has served as a member of our board of directors since November 2013. Mr. Borisy joined Third Rock Ventures, a life sciences venture capital firm focused on the formation, development and strategy of new companies, in 2009, and has been a partner since 2010. He co-founded Foundation Medicine, Inc., a public molecular information company, in 2009 and served as its interim Chief Executive Officer through May 2011; he currently serves as chairman. Mr. Borisy also co-founded Blueprint Medicines Corporation, a public oncology company, in 2010, served as its interim chief executive officer from 2013 to 2014, and he currently serves on its board of directors. In addition, since 2011, Mr. Borisy has served as chairman of Warp Drive Bio, LLC, a private life sciences company focusing on genomics, where he served as chief executive officer from 2011 to July 2013. Mr. Borisy also serves on the board of

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directors of Magenta Therapeutics, Inc., a private biotechnology company, Relay Therapeutics, Inc., a private biotechnology company, Revolution Medicines, Inc., a private company focused on the discovery and development of innovative drugs derived from natural compounds, and Tango Therapeutics, Inc., a private biotechnology and drug development company. From 2007 through 2012, Mr. Borisy served as chairman of FORMA Therapeutics, Inc., a private life science company focused on targeting cancers for treatment. In 2000, Mr. Borisy founded CombinatoRx, Inc. (now EPIRUS Biopharmaceuticals, Inc.), a public drug development company, and served as its chief executive officer and on its board of directors from 2000 to 2009. Mr. Borisy holds a B.S. in chemistry from the University of Chicago and an A.M. from Harvard University. We believe Mr. Borisy's experience working with and serving on the boards of directors of life sciences companies and his experience working in the venture capital industry qualifies him to serve on our board of directors.

**Douglas G. Cole, M.D.**, has served as a member of our board of directors since November 2013. Dr. Cole is a managing partner of venture firm Flagship Pioneering, where he has focused on life science investments since 2001. In the past five years, Dr. Cole has served on the boards of the following public biopharmaceutical companies: Agios Pharmaceuticals, Inc., Concert Pharmaceuticals, Inc., Receptos, Inc., which was acquired by Celgene, Inc., and Tetrphase Pharmaceuticals, Inc. He also serves or has served on the boards of directors of several private biopharmaceutical and diagnostics companies, including Avedro, Inc., Denali Therapeutics, Inc., Ensemble Therapeutics Corporation, Quanterix Corporation, Selecta Biosciences, Inc., Seventh Sense Biosystems, Inc., and Torque Therapeutics, Inc. Dr. Cole holds a B.A. in English from Dartmouth College and an M.D. from the University of Pennsylvania School of Medicine. We believe Dr. Cole's qualifications to sit on our board of directors include his substantial experience as an investor in emerging biopharmaceutical and life sciences companies, as well as his experience serving on the board of directors for several biopharmaceutical companies.

**John D. Mendlein, Ph.D., J.D.**, joined our board of directors in January 2016. Since July 2010, he has served as Executive Chairman of aTyr Pharma, Inc., or aTyr, a public biopharmaceutical company, and since September 2011, he has also served as aTyr's Chief Executive Officer. Dr. Mendlein is Vice Chairman of the Board of Fate Therapeutics, Inc., a public biopharmaceutical company, and also serves on the boards of directors of Moderna Therapeutics, Inc. and Pronutra Biosciences, Inc., both private biopharmaceutical companies, and BIO (Biotechnology Industry Organization) emerging companies board. From 2005 to 2008, Dr. Mendlein served as the Chief Executive Officer of Adnexus Therapeutics, Inc., a private biopharmaceutical company, which was purchased by Bristol-Myers Squibb Company in 2008. Dr. Mendlein also served on the board of directors of Monogram Biosciences, Inc., then a public HIV and oncology diagnostic company that was acquired by Laboratory Corporation of America Holdings in 2009. Before that, he served as Chairman and Chief Executive Officer of Affinium Pharmaceuticals, Ltd., a private specialty pharmaceutical company (acquired by Debiopharm Group), from 2000 to 2005, and as a director, General Counsel, and Chief Knowledge Officer at Aurora Bioscience Corporation, then a public drug discovery company (acquired by Vertex Pharmaceuticals), from August 1996 to September 2001. Dr. Mendlein holds a Ph.D. in physiology and biophysics from the University of California, Los Angeles, a J.D. from the University of California, Hastings College of the Law, and a B.S. in biology from the University of Miami. We believe that Dr. Mendlein's experience working as an executive for, and serving on the boards of directors of, numerous public and private life sciences companies qualifies him to serve as a member of our board of directors.

**Boris Nikolic, M.D.**, has served as a member of our board of directors since August 2015. Dr. Nikolic has served as managing partner of investment fund bng0, LLC since February 2015 and has served as Managing Partner of investment fund Biomatics Capital since April 2014. From April 2009 to April 2014, he served as Chief Advisor for Science and Technology to Bill Gates at bgC3, a think tank. From 2002 to 2010, Dr. Nikolic was an assistant professor at Harvard Medical School. Dr. Nikolic earned his M.D. from the Zagreb Medical School in Zagreb, Croatia. He has currently serves on the board of directors of Digitsight Technologies, Inc., a private software company, and Omniome, Inc., a private biotechnology company. He previously served on the board of directors of Schrödinger, LLC, a private chemical simulation software company, and BlueTalon, Inc., a private software company. We believe Dr. Nikolic's qualifications to sit on our board of directors include his substantial experience as an investor in life sciences companies, as well as his medical experience.

**Akshay K. Vaishnav, M.D., Ph.D.** has served as a member of our board of directors since July 2016. Dr. Vaishnav has served as the Executive Vice President of Research and Development of Alnylam

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Pharmaceuticals, Inc., or Alnylam, which develops RNA-based therapies, since December 2014 and as Chief Medical Officer of Alnylam since June 2011. Prior to that, Dr. Vaishnav held a variety of positions at Alnylam, including Senior Vice President, Clinical Research from 2008 to 2011 and Vice President, Clinical Research from 2006 to 2007. Since December 2014, Dr. Vaishnav has served as a director of Visterra, Inc., a private biopharmaceutical company focused on antibody-based therapies. From 1998 to 2005, Dr. Vaishnav held various positions at Biogen, Inc. (formerly Biogen Idec, Inc.), a biopharmaceutical company. Dr. Vaishnav is a Fellow of the Royal College of Physicians, United Kingdom. He received his M.D. from University of Wales College of Medicine and his Ph.D. from the University of London. We believe Dr. Vaishnav's qualifications to sit on our board of directors include his strong medical background and experience as an executive.

### **Family Relationships**

There are no family relationships among any of our directors or executive officers.

### **Audit Committee**

The members of our audit committee are Alexis Borisy, Douglas G. Cole, M.D., and Boris Nikolic, M.D. Mr. Borisy is the chair of our audit committee. Our board of directors has determined that each of Mr. Borisy and Drs. Cole and Nikolic is independent within the meaning of Rule 10A-3 under the Exchange Act. Our board of directors has determined that we do not have an "audit committee financial expert" as defined by applicable SEC rules serving on our audit committee. Our board of directors believes that, given the size and stage of development of our company, an audit committee financial expert is not necessary at this time because the collective financial and business expertise of the members of the audit committee is sufficient to satisfy the functions of the audit committee under the terms of the audit committee charter. In making this determination, our board of directors has considered the formal education and nature and scope of our audit committee members' previous experience, coupled with past and present service on various audit committees. Our audit committee assists our board of directors in its oversight of our accounting and financial reporting process and the audits of our consolidated financial statements. Our audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of the registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly consolidated financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures, and code of business conduct and ethics;
- overseeing our internal audit function, if any;
- discussing our risk management policies;
- establishing procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, our independent registered public accounting firm, and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by SEC rules.

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All audit services to be provided to us and all non-audit services, other than *de minimis* non-audit services, to be provided to us by our registered public accounting firm must be approved in advance by our audit committee.

### **Section 16(a) Beneficial Ownership Reporting Compliance**

Section 16(a) of the Exchange Act requires our directors, executive officers and beneficial owners of more than 10% of our common stock to file reports of holdings and transactions in our common stock and other securities of the Company with the Securities Exchange Commission. Based solely on our review of copies of such forms that we have received, or written representations from reporting persons, we believe that during the fiscal year ended December 31, 2016, all executive officers, directors and greater than 10% stockholders complied with all applicable filing requirements under Section 16(a) of the Exchange Act.

### **Code of Business Conduct and Ethics**

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 copy of the code is posted on the Corporate Governance section of our website, which is located at [www.editasmedicine.com](http://www.editasmedicine.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.

### **Item 11. Executive Compensation.**

This section discusses the material elements of our executive compensation policies for our “named executive officers” and the most important factors relevant to an analysis of these policies. It provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our executive officers named in the “Summary Compensation Table” below, or our “named executive officers,” and is intended to place in perspective the data presented in the following tables and the corresponding narrative.

#### **2016 Summary Compensation Table**

The following table sets forth information regarding compensation earned by our President and Chief Executive Officer during the year ended December 31, 2015 and by our President and Chief Executive Officer, Chief Scientific Officer and Chief Medical Officer during the year ended December 31, 2016.

<b>Name and Principal Position</b>	<b>Year</b>	<b>Salary (\$)</b>	<b>Option Awards (\$)<sup>(1)</sup></b>	<b>Non-Equity Incentive Plan Compensation (\$)<sup>(2)</sup></b>	<b>Total (\$)</b>
Katrine S. Bosley <sup>(3)</sup>	2016	450,000	429,255	222,750	1,102,005
<i>President and Chief Executive Officer</i>	2015	386,200	—	121,653	507,853
Charles Albright, Ph.D. <sup>(4)</sup>	2016	136,538	2,506,028	44,297	2,686,863
<i>Chief Scientific Officer</i>					
Gerald Cox, M.D., Ph.D.	2016	100,000	2,367,450	—	2,467,450
<i>Chief Medical Officer<sup>(5)</sup></i>					

- (1) Reflects the aggregate grant date fair value of stock and option awards granted during the year in question calculated in accordance with the provisions of Financial Accounting Standards Board Accounting Standard Codification Topic 718, *Compensation—Stock Compensation*. See Note 10 to our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards.

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- (2) 2016 amounts represent a cash bonus award earned by our President and Chief Executive Officer and our Chief Scientific Officer during 2016 to be paid to each of them in 2017. 2015 amounts represent a cash bonus award earned by our President and Chief Executive Officer during 2015 and paid to her in 2016.
- (3) Ms. Bosley also serves as a member of our board of directors but does not receive any additional compensation for her service as a director.
- (4) Dr. Albright's employment commenced with us in August 2016. The 2016 salary and non-equity incentive plan compensation amounts reported reflect the pro rata portion of Dr. Albright's annual salary of \$375,000 from commencement of his employment through December 31, 2016 and a pro rated bonus.
- (5) Dr. Cox's employment commenced with us in October 2016. The 2016 salary reported reflects the pro rata portion of Dr. Cox's annual salary of \$400,000 from commencement of his employment through December 31, 2016. Dr. Cox was not eligible for a bonus in 2016 due to his start date occurring in the fourth quarter of 2016.

### **Narrative Disclosure to Summary Compensation Table**

*Base Salary.* In 2016, we paid an annual base salary of \$450,000 to Ms. Bosley and \$136,538 and \$100,000 to Drs. Albright and Cox, which represents a pro rata portion of an annual base salary of \$375,000 and \$400,000, respectively. In 2015, we paid an annual base salary of \$386,200 to Ms. Bosley. We use base salaries to recognize the experience, skills, knowledge, and responsibilities required of all our employees, including our named executive officers. None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary.

*Annual Bonus.* Our board of directors may, in its discretion, award bonuses to our named executive officers from time to time. We typically establish annual bonus targets based around a set of specified corporate goals for our named executive officers and conduct an annual performance review to determine the attainment of such goals. Our management may propose bonus awards to our board of directors primarily based on such review process. Our board of directors makes the final determination of the eligibility requirements for and the amount of such bonus awards. Under the terms of their respective offer letters, each of our named executive officers is eligible to receive an annual cash bonus, as determined by our board of directors in its sole discretion, with a target of a specified percentage of such officer's annual base salary earned in such particular calendar year, which percentage shall be subject to adjustment from time to time by our board of directors in its sole discretion. Our board of directors determines the amount of the bonus, if any, based on its assessment of the named executive officer's performance and that of the company against appropriate goals established annually by our board of directors. The current target annual bonus percentage for each of our named executive officers is 55%, 35% and 35% for Ms. Bosley, Dr. Albright and Dr. Cox, respectively. With respect to 2016, we awarded a bonus of \$222,750 to Ms. Bosley and a bonus of \$44,297 to Dr. Albright based on our achievement of certain company goals and, in the case of Dr. Albright, achievement of individual goals. Dr. Albright's 2016 bonus was pro rated due to Dr. Albright's employment commencing in the third quarter of 2016. Dr. Cox was not eligible for a bonus in 2016 due to his start date occurring in the fourth quarter of 2016. With respect to 2015, we awarded a bonus of \$121,653 to Ms. Bosley based on our achievement of certain company goals.

*Equity Incentives.* Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incentivizes our executive officers to remain in our employment during the vesting period. Accordingly our board of directors periodically reviews the equity incentive compensation of our named executive officers and from time to time may grant equity incentive awards to them in the form of stock options.

In 2016, we granted options to purchase an aggregate of 38,461, 225,000 and 225,000 shares of common stock to Ms. Bosley, Dr. Albright and Dr. Cox, respectively. We did not make any equity awards to Ms. Bosley in 2015.



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We typically grant stock option awards at the start of employment to each executive and our other employees. In 2017, we adopted an annual grant process and we retain discretion to provide additional targeted grants in certain circumstances.

We award our stock options on the date our board of directors approves the grant. We set the option exercise price and grant date fair value based on our per-share estimated valuation on the date of grant. For grants in connection with initial employment, vesting begins on the initial date of employment. Time vested stock option grants to our executives and other employees typically vest 25% on the first anniversary of grant or, if earlier, the initial employment date and in equal monthly installments thereafter, through the fourth anniversary of the vesting commencement date, and have a term of ten years from the grant date.

### Outstanding Equity Awards at 2016 Fiscal Year End

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2016.

Name	Option Awards				Stock Awards	
	Number of securities underlying unexercised options (#) exercisable	Number of securities underlying unexercised options (#) unexercisable	Option exercise price (\$)	Option expiration date	Number of shares or units of stock that have not vested (#)	Market value of shares or units of stock that have not vested \$(1)
Katrine S. Bosley	—	38,461 <sup>(1)</sup>	16.00	2/2/2026	511,112 <sup>(2)</sup>	8,295,348
Charles Albright, Ph.D.	—	225,000 <sup>(3)</sup>	16.51	9/8/2026	—	—
Gerald Cox, M.D., Ph.D.	—	225,000 <sup>(4)</sup>	15.48	10/4/2026	—	—

- (1) This option was granted on February 3, 2016. 25% of the shares vested February 2, 2017, and the remaining 75% of the shares are scheduled to vest in equal monthly installments on the second day of each month February 2, 2020.
- (2) 1,362,966 shares of restricted common stock were awarded on June 18, 2014. 25% of the shares vested on June 16, 2015, and the remaining 75% of the shares are scheduled to vest in equal monthly installments thereafter until June 18, 2018.
- (3) This option was granted on September 9, 2016. 25% of the shares are scheduled to vest on August 22, 2017, and the remaining 75% of the shares are scheduled to vest in equal monthly installments thereafter until August 22, 2020.
- (4) This option was granted on October 5, 2016. 25% of the shares are scheduled to vest on October 3, 2017, and the remaining 75% of the shares are scheduled to vest in equal monthly installments thereafter until October 3, 2020.

### Agreements with our Executive Officers

We have entered into written offer letters with each of our named executive officers. These agreements set forth the terms of the named executive officer's compensation, including his or her initial base salary, and an annual cash bonus opportunity. In addition, the offer letters provide that the named executive officers are eligible to participate in company-sponsored benefit programs that are available generally to all of our employees.

### Potential Payments upon Termination or Change in Control

Our severance benefits plan, which we refer to as the Severance Plan, provides severance benefits to certain of our executives, including our named executive officers, and other employees designated by our board of directors or an authorized committee thereof, if their employment is terminated by us "without cause" or, only in connection with a

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“change in control” of our company, they terminate employment with us for “good reason” (as each of those terms is defined in the Severance Plan).

Under the Severance Plan, if we terminate an eligible executive’s employment without cause prior to or more than 12 months following the closing of a change in control of our company, the executive is entitled to (a) continue receiving his or her base salary for a specified period (in the case of our Chief Executive Officer, other C-level officers, and Senior Vice Presidents, for 12 months, and, in the case of Vice Presidents, for six months) following the date of termination, which we refer to as the Severance Period, (b) company contributions to the cost of health care continuation under the Consolidated Omnibus Budget Reconciliation Act, or COBRA, for the Severance Period, and (c) the amount of any unpaid annual bonus determined by our board of directors to be payable to the executive for any completed bonus period which ended prior to the date of such executive’s termination.

The Severance Plan also provides that, if, within 12 months following the closing of a change in control of our company, we terminate an eligible executive’s employment without cause or such executive terminates his or her employment with us for good reason, each of which events we refer to as a Change in Control Termination, the executive is entitled to (a) continue receiving his or her base salary for a specified period (in the case of our Chief Executive Officer, other C-level officers, and Senior Vice Presidents, for 12 months, and, in the case of Vice Presidents, for nine months) following the date of termination, which we refer to as the Change in Control Severance Period, (b) company contributions to the cost of health care continuation under COBRA during the Change in Control Severance Period, (c) the amount of any unpaid annual bonus determined by our board of directors to be payable to the executive for any completed bonus period which ended prior to the date of such executive’s termination, and (d) an additional single lump sum bonus payment in an amount equal to the multiple of (i) a fraction the numerator of which is the numbers of months in the Change in Control Severance Period and the denominator of which is 12 and (ii) the eligible executive’s target annual bonus for the year of the Change in Control Termination. In addition, in the event of a Change in Control Termination, all of the executive’s outstanding unvested equity awards will immediately vest in full on the date of such termination.

All payments and benefits provided under the Severance Plan are contingent upon the execution and effectiveness of a release of claims by the executive in our favor and continued compliance by the executive with any proprietary information and inventions, nondisclosure, non-competition, and non-solicitation (or similar) agreement to which we and the executive are party.

Ms. Bosley and Drs. Albright and Cox are entitled to severance benefits pursuant to the Severance Plan. Additionally, if Ms. Bosley terminates her employment for good reason at a time that is prior to or more than 12 months following a change in control of our company, she is entitled, pursuant to the terms of her offer letter, to (i) continue receiving her base salary for a period of 12 months following the date of termination and (ii) company contributions to the cost of health care continuation under COBRA for 12 months.

### **Other Agreements**

We have also entered into employee confidentiality, non-solicitation, non-competition and proprietary information agreements with each of our named executive officers. Under these agreements, each of our named executive officers has agreed (1) not to compete with us during his or her employment and for a period of one year after the termination of his or her employment, (2) not to solicit our employees during his or her employment and for a period of one year after the termination of his or her employment, (3) to protect our confidential and proprietary information, and (4) to assign to us related intellectual property developed during the course of his or her employment.

### **Stock Option and Other Compensation Plans**

The three equity incentive plans described in this section are our 2013 Stock Incentive Plan, as amended to date, or the 2013 plan; our 2015 Stock Incentive Plan, or the 2015 plan; and our 2015 Employee Stock Purchase Plan, or the 2015 ESPP. Prior to our initial public offering, or IPO, we granted awards to eligible participants under the 2013 plan. In connection with our IPO, we ceased granting awards under the 2013 plan and started granting awards to eligible

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participants under the 2015 plan and the 2015 ESPP. Awards granted under the 2013 plan prior to our initial public offering remain outstanding under the 2013 plan.

**2013 Stock Incentive Plan**

The 2013 plan provided for the grant of incentive stock options, nonqualified stock options, restricted stock awards, restricted stock units, stock appreciation rights, and other stock-based awards. Our employees, officers, directors, consultants, and advisors were eligible to receive awards under the 2013 plan; however, incentive stock options could only be granted to our employees. Our board of directors administers the 2013 plan.

The 2013 plan provided that a maximum of 6,317,769 shares of our common stock were authorized for issuance under the plan. No awards could be granted under the 2013 plan after November 20, 2023, and our board of directors may amend, suspend, or terminate the 2013 plan at any time.

Upon the occurrence of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spinoff, or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, under the terms of the 2013 plan, we are required to equitably adjust (or make substitute awards, if applicable), in the manner determined by our board of directors:

- the number and class of securities available under the 2013 plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and the measurement price of each outstanding stock appreciation right;
- the number of shares subject to and the repurchase price per share subject to each outstanding restricted stock award; and
- the share and per-share-related provisions and the purchase price, if any, of each outstanding other stock-based award.

Upon the occurrence of a merger or consolidation of our company with or into another entity as a result of which all of our common stock is converted into or exchanged for the right to receive cash, securities, or other property or is cancelled; any transfer or disposition of all of our common stock for cash, securities, or other property pursuant to a share exchange or other transaction; or a liquidation or dissolution of our company, our board of directors may, on such terms as our board of directors determines (except to the extent specifically provided otherwise in an applicable award agreement or other agreement between us and the plan participant), take any one or more of the following actions pursuant to the 2013 plan, as to some or all outstanding awards, other than restricted stock awards:

- provide that awards shall be assumed, or substantially equivalent awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to a plan participant, provide that the participant's unexercised awards will terminate immediately prior to the consummation of such transaction unless exercised by the participant (to the extent then exercisable) within a specified period;
- provide that outstanding awards shall become exercisable, realizable, or deliverable, or restrictions applicable to an award shall lapse, in whole or in part prior to or upon such transaction;
- in the event of a transaction under the terms of which holders of common stock will receive upon consummation thereof a cash payment for each share surrendered in the transaction, make or provide for a cash payment to a plan participant;

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- provide that, in connection with a liquidation or dissolution of the company, awards shall convert into the right to receive liquidation proceeds; or
- any combination of the foregoing.

Our board of directors is not obligated under the 2013 plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

Upon the occurrence of any corporate transaction described above, other than our liquidation or dissolution, our repurchase and other rights under each outstanding restricted stock award will continue for the benefit of our successor and will, unless our board of directors determines otherwise, apply to the cash, securities, or other property which our common stock was converted into or exchanged for in the transaction in the same manner and to the same extent as they applied to the common stock subject to the restricted stock award; provided, however, that the board may provide termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement, either initially or by amendment. Upon our liquidation or dissolution, except to the extent specifically provided to the contrary in the restricted stock award agreement or any other agreement between the plan participant and us, all restrictions and conditions on all restricted stock awards then outstanding will automatically be deemed terminated or satisfied.

Our board of directors, in its sole discretion, may accelerate the exercisability of any option or time at which any restrictions shall lapse or be removed from any restricted stock award, as the case may be.

As of January 1, 2017, there were options to purchase 1,595,082 shares of our common stock outstanding under the 2013 plan, at a weighted average exercise price of \$6.54 per share, and options to purchase 162,870 shares of our common stock had been exercised. We have awarded 1,691,137 shares of restricted common stock under the 2013 plan. We will grant no further stock options or other awards under the 2013 plan.

### ***2015 Stock Incentive Plan***

The 2015 plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, awards of restricted stock, restricted stock units, and other stock-based awards. As of January 1, 2017, 4,226,980 shares of our common stock were reserved for issuance under the 2015 plan, which included 2,868,680 shares that were formerly available for grant or reserved for issuance pursuant to awards previously outstanding under the 2013 plan and 1,466,508 shares that were authorized for issuance under the 2015 plan as of January 1, 2017 in accordance with the terms of the 2015 plan. The number of shares reserved for issuance under the 2015 plan is subject to further increases for (a) any additional shares of our common stock subject to outstanding awards under the 2013 plan that expire, terminate, or are otherwise surrendered, cancelled, forfeited, or repurchased by us at their original issuance price pursuant to a contractual repurchase right and (b) additional annual increases, to be added as of the first day of each fiscal year, from January 1, 2018 until, and including, January 1, 2026, equal to the lowest of 2,923,076 shares of our common stock, 4% of the number of shares of our common stock outstanding on such first day of the fiscal year in question and an amount determined by our board of directors.

Our employees, officers, directors, consultants, and advisors are eligible to receive awards under the 2015 plan; however, incentive stock options may only be granted to our employees.

Pursuant to the terms of the 2015 plan, our board of directors (or a committee delegated by our board of directors) administers the 2015 plan and, subject to any limitations set forth in the 2015 plan, will select the recipients of awards and determine:

- the number of shares of common stock covered by options and the dates upon which those options become exercisable;
- the type of options to be granted;

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- the exercise price of options, which price must be at least equal to the fair market value of our common stock on the date of grant;
- the duration of options, which may not be in excess of ten years;
- the methods of payment of the exercise price of options; and
- the number of shares of our common stock subject to and the terms of any stock appreciation rights, awards of restricted stock, restricted stock units, or other stock-based awards and the terms and conditions of such awards, including the issue price, conditions for repurchase, repurchase price, and performance conditions (though the measurement price of stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of such awards may not be in excess of ten years), if any.

Our board of directors may delegate authority to an executive officer to grant awards under the 2015 plan to all of our employees, except executive officers and certain other officers provided that our board of directors fixes the terms of the awards to be granted by such executive officer, including the exercise price of such awards (or a formula for establishing such price), and the maximum number of shares subject to awards that such executive officer may make.

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off, or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, we are required by the 2015 plan to make equitable adjustments (or make substitute awards, if applicable), in a manner determined by our board of directors, to:

- the number and class of securities available under the 2015 plan;
- the share counting rules under the 2015 plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and measurement price of each outstanding stock appreciation right;
- the number of shares and the repurchase price per share subject to each outstanding restricted stock award or restricted stock unit award; and
- the share and per-share related provisions and purchase price, if any, of any outstanding other stock-based award.

Upon a reorganization event (as defined in the 2015 plan), our board of directors, may, on such terms as our board of directors determines (except to the extent specifically provided otherwise in an applicable award agreement or other agreement between the participant and us), take any one or more of the following actions pursuant to the 2015 plan, as to some or all outstanding awards, other than restricted stock awards:

- provide that all outstanding awards will be assumed or substantially equivalent awards will be substituted by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to a participant, provide that the participant's unvested and/or unexercised options or other awards will terminate immediately prior to the consummation of the reorganization event unless exercised by the participant;
- provide that outstanding awards will become exercisable, realizable, or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon the reorganization event;

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- in the event of a reorganization event pursuant to which holders of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to the participants with respect to each award held by a participant equal to (a) the number of shares of our common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (b) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement, or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award;
- provide that, in connection with a liquidation or dissolution, awards convert into the right to receive liquidation proceeds (if applicable, net of exercise, measurement, or purchase price thereof and any applicable tax withholdings); or
- any combination of the foregoing.

Our board of directors is not obligated by the 2015 plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than a liquidation or dissolution, the repurchase and other rights of our company with respect to each outstanding restricted stock award will continue for the benefit of the successor company and will, unless our board of directors may otherwise determine, apply to the cash, securities, or other property into or for which our common stock is converted or exchanged pursuant to the reorganization event, unless our board of directors provides for the termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement or any other agreement between the participant and us. Upon the occurrence of a reorganization event involving a liquidation or dissolution, all restrictions and conditions on each outstanding restricted stock award will automatically be deemed terminated or satisfied, unless otherwise provided in the agreement evidencing the restricted stock award or in any other agreement between the participant and us.

Our board of directors may at any time provide that any award under the 2015 plan shall become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

No award may be granted under the 2015 plan after February 1, 2026. Our board of directors may amend, suspend, or terminate the 2015 plan at any time, except that stockholder approval will be required to comply with applicable law or stock market requirements.

As of January 1, 2017, there were options to purchase 1,569,746 shares of our common stock outstanding under the 2015 plan, at a weighted-average exercise price of \$20.92 per share, and no options to purchase shares of our common stock had been exercised.

### ***2015 Employee Stock Purchase Plan***

The 2015 ESPP is administered by our board of directors or by a committee appointed by our board of directors. As of January 1, 2017, 751,242 shares of our common stock were reserved for issuance under the 2015 ESPP, which included 366,627 shares that were authorized for issuance under the 2015 ESPP as of January 1, 2017 in accordance with the terms of the 2015 ESPP. The number of shares reserved for issuance under the 2015 ESPP is subject to additional annual increases, to be added as of the first day of each fiscal year, from January 1, 2018 until, and including, January 1, 2026, in an amount equal to the least of (a) 769,230 shares of our common stock, (b) 1% of the total number of shares of our common stock outstanding on the first day of the applicable year, and (c) an amount determined by our board of directors.

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All of our employees or employees of any designated subsidiary, as defined in the 2015 ESPP, are eligible to participate in the 2015 ESPP, provided that:

- such person is customarily employed by us or a designated subsidiary for more than 20 hours a week and for more than five months in a calendar year;
- such person has been employed by us or by a designated subsidiary for at least six months prior to enrolling in the 2015 ESPP; and
- such person was our employee or an employee of a designated subsidiary on the first day of the applicable offering period under the 2015 ESPP.

No employee may purchase shares of our common stock under the 2015 ESPP and any of our other employee stock purchase plans in excess of \$25,000 of the fair market value of our common stock (as of the date of the option grant) in any calendar year. In addition, no employee may purchase shares of our common stock under the 2015 ESPP that would result in the employee owning 5% or more of the total combined voting power or value of our stock or the stock of any of our subsidiaries.

We expect to make one or more offerings to our eligible employees to purchase stock under the 2015 ESPP beginning at such time as our board of directors may determine. Each offering will consist of a six-month offering period during which payroll deductions will be made and held for the purchase of our common stock at the end of the offering period. Our board of directors or a committee designated by the board of directors may, at their discretion, choose a different period of not more than 12 months for offerings.

On the commencement date of each offering period, each eligible employee may authorize up to a maximum of 15% of his or her compensation to be deducted by us during the offering period. Each employee who continues to be a participant in the 2015 ESPP on the last business day of the offering period will be deemed to have exercised an option to purchase from us the number of whole shares of our common stock that his or her accumulated payroll deductions on such date will pay for, not in excess of the maximum numbers set forth above. Under the terms of the 2015 ESPP, the purchase price shall be determined by our board of directors for each offering period and will be at least 85% of the applicable closing price of our common stock. If our board of directors does not make a determination of the purchase price, the purchase price will be 85% of the lesser of the closing price of our common stock on the first business day of the offering period or on the last business day of the offering period.

An employee who is not a participant on the last day of the offering period is not entitled to purchase shares under the 2015 ESPP, and the employee's accumulated payroll deductions will be refunded. An employee's rights under the 2015 ESPP terminate upon voluntary withdrawal from an offering under the 2015 ESPP at any time, or when the employee ceases employment for any reason.

We will be required to make equitable adjustments to the number and class of securities available under the 2015 ESPP, the share limitations under the 2015 ESPP, and the purchase price for an offering period under the 2015 ESPP to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combinations of shares, reclassifications of shares, spin-offs and other similar changes in capitalization or events or any dividends or distributions to holders of our common stock other than ordinary cash dividends.

In connection with a reorganization event, as defined in the 2015 ESPP, our board of directors or a committee of our board of directors may take any one or more of the following actions as to outstanding options to purchase shares of our common stock under the 2015 ESPP on such terms as our board or committee determines:

- provide that options shall be assumed, or substantially equivalent options shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to employees, provide that all outstanding options will be terminated immediately prior to the consummation of such reorganization event and that all such outstanding options will become

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exercisable to the extent of accumulated payroll deductions as of a date specified by our board or committee in such notice, which date shall not be less than ten days preceding the effective date of the reorganization event;

- upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the reorganization event and that all accumulated payroll deductions will be returned to participating employees on such date;
- in the event of a reorganization event under the terms of which holders of our common stock will receive upon consummation thereof a cash payment for each share surrendered in the reorganization event, change the last day of the offering period to be the date of the consummation of the reorganization event and make or provide for a cash payment to each employee equal to (a) the cash payment for each share surrendered in the reorganization event times the number of shares of our common stock that the employee's accumulated payroll deductions as of immediately prior to the reorganization event could purchase at the applicable purchase price, where the acquisition price is treated as the fair market value of our common stock on the last day of the applicable offering period for purposes of determining the purchase price and where the number of shares that could be purchased is subject to the applicable limitations under the 2015 ESPP minus (b) the result of multiplying such number of shares by the purchase price; and/or
- provide that, in connection with our liquidation or dissolution, options shall convert into the right to receive liquidation proceeds (net of the purchase price thereof).

Our board of directors may at any time, and from time to time, amend or suspend the 2015 ESPP or any portion thereof. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Internal Revenue Code. Further, our board of directors may not make any amendment that would cause the 2015 ESPP to fail to comply with Section 423 of the Internal Revenue Code. The 2015 ESPP may be terminated at any time by our board of directors. Upon termination, we will refund all amounts in the accounts of participating employees.

As of the date of the filing of this Annual Report on Form 10-K, we had not made any offerings or issued any shares under the 2015 ESPP.

### **Inducement Grant**

In connection with hiring Dr. Cox, our board of directors approved an inducement grant of an option to purchase up to 225,000 shares of our common stock, with an exercise price of \$15.48 per share, which was equal to the closing price per share of our common stock on the date of grant. The option is scheduled to vest over four years, with 25% of the shares scheduled to vest on October 3, 2017, and the remainder scheduled to vest ratably at the end of each subsequent month thereafter through October 3, 2020, subject to Dr. Cox's continued service relationship with our company through the applicable vesting dates.

### **401(k) Retirement Plan**

We maintain a 401(k) retirement plan that is intended to be a tax-qualified defined contribution plan under Section 401(k) of the Internal Revenue Code. In general, all of our employees are eligible to participate promptly following commencement of their employment. The 401(k) plan includes a salary deferral arrangement pursuant to which participants may elect to reduce their current compensation by up to the statutorily prescribed limit, equal to \$18,000 in 2017, and have the amount of the reduction contributed to the 401(k) plan. We provide a 200% match of employee contributions under our 401(k) plan, up to a limit on our contributions of the lesser of \$6,000 and 3% of the employee's salary.



### **Limitation of Liability and Indemnification**

Our restated certificate of incorporation limits the liability of directors to the maximum extent permitted by Delaware law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for breaches of their fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any unlawful payments related to dividends or unlawful stock repurchases, redemptions, or other distributions; or
- any transaction from which the director derived an improper personal benefit.

These limitations do not apply to liabilities arising under federal securities laws and do not affect the availability of equitable remedies, including injunctive relief or rescission. If Delaware law is amended to authorize the further elimination or limiting of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law as so amended.

As permitted by Delaware law, our restated certificate of incorporation also provides that:

- we will indemnify our directors and officers to the fullest extent permitted by law;
- we may indemnify our other employees and other agents to the same extent that we indemnify our officers and directors, unless otherwise determined by our board of directors; and
- we will advance expenses to our directors and officers in connection with legal proceedings in connection with a legal proceeding to the fullest extent permitted by law.

The indemnification provisions contained in our restated certificate of incorporation are not exclusive. In addition, we have entered into indemnification agreements with our directors and our executive officers, including our named executive officers. These indemnification agreements require us, among other things, to indemnify each such director for some expenses, including attorneys' fees, judgments, fines, and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our directors or as one of our officers.

We believe that these provisions and agreements are necessary to attract and retain qualified persons as directors and officers. Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, or the Securities Act, may be permitted to directors, officers, or persons controlling our company pursuant to the foregoing provisions, we understand that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

In addition, we maintain standard policies of insurance under which coverage is provided to our directors and officers against losses arising from claims made by reason of breach of duty or other wrongful act, and to us with respect to payments which may be made by us to such directors and officers pursuant to the above indemnification provisions or otherwise as a matter of law.

### **Rule 10b5-1 Sales Plans**

Certain of our executive officers have adopted, and other directors and executive officers may in the future adopt, written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer.

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The director or officer may amend or terminate the plan in some circumstances. Our directors and executive officers may also buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

**Director Compensation**

We do not pay any compensation to our President and Chief Executive Officer in connection with her service on our board of directors. The compensation that we pay to our President and Chief Executive Officer is discussed earlier in this “Executive Compensation” section.

Under our director compensation program, we pay our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chairman of the board and of each committee receive higher retainers for such service. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of such quarter that the director is not serving on our board of directors and no fee was payable in respect of any period prior to February 2, 2016, the effective date of the registration statement for our initial public offering. The fees paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

	<u>Member Annual Fee</u>	<u>Chairman Annual Fee</u>
Board of Directors	\$ 35,000	\$ 75,000
Audit Committee	\$ 7,500	\$ 15,000
Compensation Committee	\$ 5,000	\$ 10,000
Nominating and Corporate Governance Committee	\$ 4,000	\$ 8,000

We also reimburse our non-employee directors for reasonable travel and other expenses incurred in connection with attending our board of director and committee meetings.

In addition, under our director compensation program, each non-employee director receives under the 2015 plan, upon his or her initial election to our board of directors, an option to purchase 23,076 shares of our common stock. Each of these options vests as to one-third of the shares of our common stock underlying such option on each anniversary of the grant date until the third anniversary of the grant date, subject to the non-employee director’s continued service as a director. Further, on the date of the first board meeting held after each annual meeting of stockholders, each non-employee director that has served on our board of directors for at least six months receives, under the 2015 plan, an option to purchase 11,538 shares of our common stock. Each of these options will vest in full on the one-year anniversary of the grant date unless otherwise provided at the time of grant, subject to the non-employee director’s continued service as a director. All options issued to our non-employee directors under our director compensation program are issued at exercise prices equal to the fair market value of our common stock on the date of grant and become exercisable in full upon a change in control of our company.

The following table sets forth information regarding compensation earned by our non-employee directors during the year ended December 31, 2016. There were no outstanding equity awards held by our non-employee directors as of December 31, 2016 other than the options described in footnotes (2) and (3) to the following table.

<u>Name</u>	<u>Fees earned or paid in cash (\$)</u>	<u>Option awards (\$)<sup>(1)</sup></u>	<u>Total (\$)</u>
Kevin Bitterman, Ph.D.	43,217	—	43,217
Alexis Borisy	45,492	—	45,492
Douglas G. Cole, M.D.	40,032	—	40,032
John D. Mendlein, Ph.D., J.D.	48,221	1,073,067 <sup>(2)</sup>	1,121,288
Boris Nikolic, M.D.	42,307	—	42,307
Akshay K. Vaishnav, M.D., Ph.D. <sup>(3)</sup>	15,014	424,679 <sup>(4)</sup>	439,693

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- (1) Reflects the aggregate grant date fair value of option awards granted during the year in question calculated in accordance with the provisions of Financial Accounting Standards Board Accounting Standard Codification Topic 718, *Compensation—Stock Compensation*. See Note 10 to our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards.
- (2) This option was granted on February 3, 2016 in connection with Dr. Mendlein’s election to our Board of Directors. The 96,153 shares subject to the option are scheduled to vest over three years in equal monthly installments of one thirty-sixth of the shares beginning on February 24, 2016 through January 24, 2019.
- (3) Dr. Vaishnaw joined our board of directors in July 2016.
- (4) This option was granted on July 28, 2016 in connection with Mr. Vaishnaw’s election to our Board of Directors. The 23,076 shares subject to the option are scheduled to vest over three years in equal yearly installments of one-third of the shares beginning on July 28, 2017 through July 28, 2019.

### **Compensation Committee Interlocks and Insider Participation**

None of our executive officers serves as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any other entity that has one or more of its executive officers serving as a member of our board of directors or our compensation committee. None of the members of our compensation committee who served during 2016 is, or has ever been, an officer or employee of our company, other than Kevin Bitterman, who served as our President from November 2013 until June 2014 and no longer serves as a member of our compensation committee.

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

The following table sets forth information with respect to the beneficial ownership of our common stock, as of January 1, 2017 by:

- each person known by us to beneficially own more than 5% of our common stock;
- each of our directors;
- each of our named executive officers; and
- all of our executive officers and directors as a group.

The column entitled “Percentage of Shares Beneficially Owned” is based on a total of 36,662,724 shares of our common stock outstanding as of January 1, 2017.

The number of shares beneficially owned by each stockholder is determined under rules issued by the Securities and Exchange Commission and includes voting or investment power with respect to securities. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power. In computing the number of shares beneficially owned by an individual or entity and the percentage ownership of that person, shares of common stock subject to options, warrants, or other rights held by such person that are currently exercisable or will become exercisable within 60 days after January 1, 2017 are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other person. Unless otherwise indicated, the address of all listed stockholders is 11 Hurley St., Cambridge, Massachusetts 02141. Each of the stockholders listed has sole voting and investment power with respect to the shares beneficially owned by the stockholder unless noted otherwise, subject to community property laws where applicable.

Name of Beneficial Owner	Shares Beneficially Owned	Percentage of Shares Beneficially Owned
<b>5% Stockholders</b>		
Entities affiliated with FMR LLC <sup>(1)</sup>	5,498,390	15.0 %
Entities affiliated with Third Rock Ventures III, L.P. <sup>(2)</sup>	3,906,176	10.7 %
Entities affiliated with Polaris Ventures Partners VI, L.P. <sup>(3)</sup>	3,797,144	10.4 %
Entities affiliated with Flagship Ventures Management, Inc. <sup>(4)</sup>	3,455,316	9.4 %
bng0, LLC <sup>(5)</sup>	2,649,572	7.2 %
<b>Named Executive Officers and Directors</b>		
Charles Albright, Ph.D.	—	—
Katrine S. Bosley <sup>(6)</sup>	1,451,511	4.0 %
Kevin Bitterman, Ph.D. <sup>(7)</sup>	3,797,144	10.4 %
Alexis Borisy	479	*
Douglas G. Cole, M.D.	—	—
Gerald Cox, M.D., Ph.D.	—	—
John D. Mendlein, Ph.D., J.D. <sup>(8)</sup>	34,722	*
Boris Nikolic, M.D. <sup>(9)</sup>	2,649,572	7.2 %
Akshay K. Vaishnav, M.D., Ph.D.	—	—
All executive officers and directors as a group (11 persons) <sup>(10)</sup>	8,201,162	22.3 %

\* Less than 1%.

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- (1) FMR LLC reports sole voting power with respect to 677,885 shares and sole dispositive power with respect to 5,498,390 shares. Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC. Members of the Johnson family, 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 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 the 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 LLC is 245 Summer Street, Boston, Massachusetts 02210. For information regarding FMR LLC and its affiliates, we have relied on a Schedule 13G/A filed by FMR LLC with the SEC on February 14, 2017.
- (2) Consists of 3,906,176 shares of common stock held by Third Rock Ventures III, L.P., or TRV III LP. Each of (i) Third Rock Ventures III GP, L.P., or TRV III GP, the general partner of TRV III LP, (ii) Third Rock Ventures GP III, LLC, or TRV III LLC, the general partner of TRV III GP, and (iii) Mark Levin, Kevin Starr, and Robert Tepper, the managers of TRV III LLC, may be deemed to have voting and investment power over the shares held of record by TRV III LP. Each of TRV III GP, TRV III LLC, Mark Levin, Kevin Starr, and Robert Tepper disclaims beneficial ownership of such shares, except to the extent of their respective pecuniary interests therein. The address of TRV III LP is 29 Newbury Street, Suite 401, Boston, MA 02116.
- (3) Consists of (i) 3,587,501 shares of common stock held directly by Polaris Venture Partners VI, L.P. and (ii) 209,643 shares of common stock held directly by Polaris Venture Partners Founders' Fund VI, L.P., or together with Polaris Venture Partners VI, L.P., the Polaris Funds. Polaris Venture Management Co. VI, L.L.C., or Polaris Management, is the general partner of each of the Polaris Funds and may be deemed to have sole power to vote and dispose of the shares held by the Polaris Funds. Each of David Barrett, Brian Chee, Jonathan Flint, Terrance McGuire, Amir Nashat and Bryce Youngren, collectively referred to as the Managing Members, are the managing members of Polaris Management and may be deemed to share voting and dispositive power with respect to the shares held by the Polaris Funds. Dr. Bitterman, a member of our board of directors, has an assignee interest in Polaris Management and may be deemed to share voting and dispositive powers with respect to the shares held by the Polaris Funds by virtue of his relationship to Polaris Management. Each of Polaris Management, the Managing Members and Dr. Bitterman disclaim beneficial ownership of all of the shares owned by the Polaris Funds, except to the extent of their respective and proportionate pecuniary interests therein. The address of the Polaris Funds is One Marina Park Drive, 10<sup>th</sup> Floor, Boston, Massachusetts 02210.
- (4) Consists of (i) 2,764,256 shares of common stock held by Flagship Ventures Fund IV, L.P. and (ii) 691,060 shares of common stock held by Flagship Ventures Fund IV-Rx, L.P., or collectively, the Flagship Funds. Flagship Ventures Fund IV General Partner LLC, or Flagship GP, is the general partner of the Flagship Funds. Noubar B. Afeyan, Ph.D., and Edwin M. Kania, Jr. are the managers of Flagship GP. As a result, each of Flagship GP, Mr. Afeyan, and Mr. Kania may be deemed to possess voting and investment control over, and may be deemed to have indirect beneficial ownership with respect to, all shares held by the Flagship Funds. Each of Flagship GP, Mr. Afeyan, and Mr. Kania disclaims beneficial ownership of such shares, except to the extent of their respective pecuniary interests therein. Dr. Cole, a member of our board of directors, is a member of Flagship GP and does not have voting or investment control over the shares held by the Flagship Funds. Dr. Cole disclaims beneficial ownership of all shares held by the Flagship Funds, except to the extent of his pecuniary interest therein. The address of the Flagship Funds is 55 Cambridge Parkway Suite 800E, Cambridge, Massachusetts 02142.
- (5) Consists of shares of common stock held by bng0, LLC. Boris Nikolic, M.D., a member of our board of directors, is a member and the managing director of bng0, LLC. He has voting and investment power over such shares and may be deemed the indirect beneficial owner of such shares. Dr. Nikolic disclaims beneficial ownership over such shares, except to the extent of any pecuniary interest therein. The address of bng0, LLC is 1107 First Avenue, Apt. 1305, Seattle, WA 98101.

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- (6) Consists of 1,441,095 shares of common stock, of which 454,322 remain subject to vesting 60 days after January 1, 2017, and 10,416 shares of common stock issuable upon the exercise of options exercisable within 60 days after January 1, 2017.
- (7) Consists of the shares described in note (3) above. Dr. Bitterman, a member of our board of directors, has an assignee interest in Polaris Management. To the extent that he is deemed to share voting and investment powers with respect to the shares held by the Polaris Funds, Dr. Bitterman disclaims beneficial ownership of all the shares held by the funds except to the extent of his pecuniary interest therein.
- (8) Consists of 34,722 shares of common stock issuable upon the exercise of options exercisable within 60 days after January 1, 2017.
- (9) Consists of the shares described in note (5) above. Dr. Nikolic is a member and the managing director of bng0, LLC and may be deemed the indirect beneficial owner of such shares. Dr. Nikolic disclaims beneficial ownership over such shares, except the extent of his pecuniary interest therein.
- (10) Includes 471,513 shares of common stock that remain subject to vesting 60 days after January 1, 2017 and 195,084 shares of common stock issuable upon the exercise of options exercisable within 60 days after January 1, 2017.

**Securities authorized for issuance under equity compensation plans**

The following table contains information about our equity compensation plans as of December 31, 2016.

**Equity Compensation Plan Information**

Plan category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted-average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column(a)) (c)
Equity compensation plans approved by security holders <sup>(1)</sup>	3,164,828	\$ 13.67	2,760,472
Equity compensation plans not approved by security holders <sup>(2)</sup>	225,000	\$ 15.48	—
<b>Total</b>	<b>1,674,047</b>	<b>\$ 6.45</b>	<b>2,848,630</b>

- (1) Consists of our 2013 plan, 2015 plan, and 2015 ESPP. The amounts disclosed do not reflect an additional 1,466,508 shares of common stock authorized for issuance under the 2015 plan as of January 1, 2017 and an additional 366,627 shares of common stock authorized for issuance under the 2015 ESPP as of January 1, 2017, in each case in accordance with the terms of the applicable plan. The 2015 plan provides for further annual increases, to be added as of the first day of each fiscal year, from January 1, 2018 until, and including, January 1, 2026, equal to the lowest of 2,923,076 shares of our common stock, 4% of the number of shares of our common stock outstanding on such first day of the fiscal year in question and an amount determined by our board of directors. The 2015 ESPP provides for further annual increases, to be added as of the first day of each fiscal year, from January 1, 2018 until, and including, January 1, 2026, in an amount equal to the least of 769,230 shares of our common stock, 1% of the total number of shares of our common stock outstanding on the first day of the applicable year, and an amount determined by our board of directors.
- (2) Consists of a stock option award approved by our board of directors as an inducement material to an executive's acceptance of employment with us in accordance with NASDAQ Listing Rule 5635(c)(4).

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

The following is a description of transactions since January 1, 2016 to which we have been a party, and in which any of our directors, executive officers and holders of more than 5% of our voting securities and affiliates of our directors, executive officers and holders of more than 5% of our voting securities, had or will have a direct or indirect material interest. We believe that all of the transactions described below were made on terms no less favorable to us than could have been obtained from unaffiliated third parties.

**Participation in initial public offering**

In our initial public offering, funds affiliated with FMR LLC, Viking Global Investors L.P. and Deerfield Management Company, L.P., each of whom was one of our 5% stockholders at the time of our initial public offering, purchased 2,500,000, 1,000,000 and 100,000 shares of our common stock, respectively. Such purchases were made through the underwriters at the initial public offering price of \$16.00 per share for an aggregate purchase price of \$57.6 million.

**Director Affiliations**

Some of our directors are affiliated with and serve on our board of directors as representatives of entities which beneficially own or owned 5% or more of our common stock, as indicated in the table below:

<b>Director</b>	<b>Principal Stockholder</b>
Kevin Bitterman, Ph.D.	Polaris Venture Partners VI, L.P. and affiliate
Alexis Borisy	Third Rock Ventures III, L.P.
Douglas G. Cole, M.D.	Flagship Ventures Fund IV, L.P. and affiliate
Boris Nikolic, M.D.	bng0, LLC

**Sublease**

In February 2017, we entered into a sublease with Tango Therapeutics, Inc., or Tango, under which we agreed to sublease approximately 9,654 square feet of our corporate offices at 11 Hurley St., Cambridge, MA 02141 to Tango over a sublease term running from February 2017 to August 2018, with rent payments of approximately \$0.7 million per year due to us from Tango over the term of the sublease. One of our directors, Alexis Borisy, is the president and chairman of the board of directors of Tango. In addition, Mr. Borisy is a general partner of the general partner of Third Rock Ventures IV, L.P., which owns a majority of the outstanding capital stock of Tango. This arrangement was approved by the audit committee of our board of directors pursuant to the terms of our Related Person Transaction policy, discussed below.

**Investors' Rights Agreement**

We are a party to an amended and restated investors' rights agreement, or the Investors' Rights Agreement, dated as of August 4, 2015, with holders of our previously-outstanding preferred stock, including certain of our 5% stockholders and their affiliates and entities affiliated with certain of our officers and directors. The Investors' Rights Agreement provides these holders the right, subject to certain conditions, to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing.

**Employment Agreements**

See the "Executive Compensation—Agreements with our Executive Officers" section of this Annual Report on Form 10-K for a further discussion of these arrangements.

## **Indemnification of Officers and Directors**

Our restated certificate of incorporation provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we have entered into indemnification agreements with our current and former directors that may be broader in scope than the specific indemnification provisions contained in the General Corporation Law of the State of Delaware, or the DGCL. In the case of those of our directors who are affiliated with certain of our 5% stockholders or their affiliates, the indemnification agreements also provide for indemnification of the applicable 5% stockholder or affiliate.

## **Policies and Procedures for Related Person Transactions**

We have adopted a written related person transaction policy to set forth policies and procedures for the review and approval or ratification of related person transactions. This policy covers any transaction, arrangement, or relationship, or any series of similar transactions, arrangements, or relationships, in which we were or are to be a participant, the amount involved exceeds \$120,000, and a related person had or will have a direct or indirect material interest, including, without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness, and employment by us of a related person.

Our related person transaction policy contains exceptions for any transaction or interest that is not considered a related person transaction under SEC rules as in effect from time to time. In addition, the policy provides that an interest arising solely from a related person's position as an executive officer of another entity that is a participant in a transaction with us will not be subject to the policy if each of the following conditions is met:

- the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity;
- the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction with us and do not receive any special benefits as a result of the transaction; and
- the amount involved in the transaction equals less than the greater of \$200,000 or 5% of the annual gross revenue of the company receiving payment under the transaction.

The policy provides that any related person transaction proposed to be entered into by us must be reported to our Chief Financial Officer and will be reviewed and approved by our audit committee in accordance with the terms of the policy, prior to effectiveness or consummation of the transaction whenever practicable. The policy provides that if our Chief Financial Officer determines that advance approval of a related person transaction is not practicable under the circumstances, our audit committee will review and, in its discretion, may ratify the related person transaction at the next meeting of the audit committee following such transaction or following the date that such transaction comes to the attention of the Chief Financial Officer. The policy also provides that alternatively, our Chief Financial Officer may present a related person transaction arising in the time period between meetings of the audit committee to the chair of an audit committee, who will review and may approve the related person transaction, subject to ratification by the audit committee at the next meeting of the audit committee.

In addition, the policy provides that any related person transaction previously approved by the audit committee or otherwise already existing that is ongoing in nature will be reviewed by the audit committee annually to ensure that such related person transaction has been conducted in accordance with the previous approval granted by the audit committee, if any, and that all required disclosures regarding the related person transaction are made.

The policy provides that transactions involving compensation of executive officers will be reviewed and approved by our compensation committee in the manner to be specified in the charter of the compensation committee.

A related person transaction reviewed under this policy will be considered approved or ratified if it is authorized by the audit committee in accordance with the standards set forth in the policy after full disclosure of the related person's



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interests in the transaction. As appropriate for the circumstances, the policy provides that the audit committee will review and consider:

- the related person's interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person's interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of business of our company;
- whether the transaction with the related person is proposed to be, or was, entered into on terms no less favorable to us than the terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

The policy provides that the audit committee will review all relevant information available to it about the related person transaction. The policy provides that the audit committee may approve or ratify the related person transaction only if the audit committee determines that, under all of the circumstances, the transaction is in, or is not inconsistent with, our best interests. The policy provides that the audit committee may, in its sole discretion, impose such conditions as it deems appropriate on us or the related person in connection with approval of the related person transaction.

### **Director Independence**

Rule 5605 of the NASDAQ Listing Rules requires a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the NASDAQ Listing Rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Audit committee members must also satisfy independence criteria set forth in Rule 10A-3 under the Exchange Act, and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under Rule 5605(a)(2), a director will only qualify as an "independent director" if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director; and whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In January 2017, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that each of Mr. Borisy and Drs. Cole, Mendlein, Nikolic and Vaishnav is an "independent

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director” as defined under NASDAQ Listing Rules. Our board of directors has also determined that Mr. Borisy and Drs. Cole and Nikolic, who comprise our audit committee, and Drs. Cole, Mendlein and Vaishnav, who comprise our compensation committee, satisfy the independence standards for such committees established by the SEC and the NASDAQ Listing Rules, as applicable. In making such determination, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

**Item 14. Principal Accounting Fees and Services.**

The following table summarizes the fees of Ernst & Young LLP, our independent registered public accounting firm, billed us for each of the last two fiscal years.

	Year Ended	
	December 31,	
	2016	2015
Audit Fees <sup>(1)</sup>	\$452,500	\$1,251,259
Audit-Related Fees	—	—
Tax Fees <sup>(2)</sup>	12,330	7,500
All Other Fees	—	—
	<u>\$464,830</u>	<u>\$1,258,759</u>

- (1) Audit fees consist of fees billed for professional services by Ernst & Young LLP for audit and quarterly review of our consolidated financial statements and review of the registration statement on Form S-1 for our IPO, and related services that are normally provided in connection with statutory and regulatory filings or engagements.
- (2) Tax fees consist of fees for professional services performed by Ernst & Young LLP with respect to tax compliance, tax advice and tax planning.

The aggregate fees included in the Audit Fees are those fees billed for the fiscal year. The aggregate fees included in the Tax Fees are those fees billed in the fiscal year.

**Pre-Approval Policies and Procedures**

The audit committee of our board of directors has adopted policies and procedures for the pre-approval of audit and non-audit services for the purpose of maintaining the independence of our independent auditor. We may not engage our independent auditor to render any audit or non-audit service unless either the service is approved in advance by the audit committee, or the engagement to render the service is entered into pursuant to the audit committee’s pre-approval policies and procedures. Notwithstanding the foregoing, pre-approval is not required with respect to the provision of services, other than audit, review or attest services, by the independent auditor if the aggregate amount of all such services is no more than 5% of the total amount paid by us to the independent auditor during the fiscal year in which the services are provided, such services were not recognized by us at the time of the engagement to be non-audit services and such services are promptly brought to the attention of the audit committee and approved prior to completion of the audit by the audit committee.

From time to time, our audit committee may pre-approve services that are expected to be provided to us by the independent auditor during the following 12 months. At the time such pre-approval is granted, the audit committee must identify the particular pre-approved services in a sufficient level of detail so that our management will not be called upon to make a judgment as to whether a proposed service fits within the pre-approved services and, at each regularly scheduled meeting of the audit committee following such approval, management or the independent auditor shall report to the audit committee regarding each service actually provided to us pursuant to such pre-approval.

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The audit committee has delegated to its chairman the authority to grant pre-approvals of audit or non-audit services to be provided by the independent auditor. Any approval of services by the chairman of the audit committee is reported to the committee at its next regularly scheduled meeting.

**PART IV**

**Item 15. Exhibits and Financial Statement Schedules.**

(1) Financial Statements

Our consolidated financial statements are set forth in Part II, Item 8 of this Annual Report on Form 10-K and are incorporated herein by reference.

(2) Financial Statement Schedules

Schedules have been omitted since they are either not required or not applicable or the information is otherwise included herein.

(3) Exhibits

The exhibits filed as part of this Annual Report on Form 10-K are listed in the Exhibit Index immediately preceding such Exhibits, which Exhibit Index is incorporated herein by reference.

**SIGNATURES**

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

**EDITAS MEDICINE, INC.**

Dated: March 3, 2017

By: /s/ Katrine S. Bosley  
Katrine S. Bosley  
President and Chief Executive Officer

**SIGNATURES**

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

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Katrine S. Bosley</u> Katrine S. Bosley	President and Chief Executive Officer, Director (principal executive officer)	March 3, 2017
<u>/s/ Andrew A. F. Hack</u> Andrew A.F. Hack, M.D., Ph.D.	Chief Financial Officer (principal financial and accounting officer)	March 3, 2017
<u>/s/ Kevin Bitterman</u> Kevin Bitterman, Ph.D.	Director	March 3, 2017
<u>/s/ Alexis Borisy</u> Alexis Borisy	Director	March 3, 2017
<u>/s/ Douglas G. Cole</u> Douglas G. Cole, M.D.	Director	March 3, 2017
<u>/s/ John D. Mendlein</u> John D. Mendlein, Ph.D., J.D.	Director	March 3, 2017
<u>/s/ Boris Nikolic</u> Boris Nikolic, M.D.	Director	March 3, 2017
<u>/s/ Akshay K. Vaishnav</u> Akshay K. Vaishnav, M.D., Ph.D.	Director	March 3, 2017

**EXHIBIT INDEX**

Exhibit Number	Description of Exhibit	Incorporated by Reference			Exhibit Number	Filed Herewith
		Form	File No.	Date of Filing		
3.1	Restated Certificate of Incorporation of the Registrant	8-K	001-37687	2/8/2016	3.1	
3.2	Amended and Restated By-laws of the Registrant	8-K	001-37687	2/8/2016	3.2	
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1	333-208856	1/4/2016	4.1	
10.1+	Amended and Restated Investors' Rights Agreement, dated August 4, 2015, among the Registrant and the other parties thereto	S-1	333-208856	1/4/2016	10.1	
10.2+	2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.5	
10.3+	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.6	
10.4+	Form of Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.7	
10.5+	Form of Early Exercise Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.8	
10.6+	Form of Restricted Stock Agreement under 2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.9	
10.7+	2015 Stock Incentive Plan	S-1	333-208856	1/4/2016	10.10	
10.8+	Form of Incentive Stock Option Agreement under 2015 Stock Incentive Plan	S-1	333-208856	1/4/2016	10.11	
10.9+	Form of Nonstatutory Stock Option Agreement under 2015 Stock Incentive Plan	S-1	333-208856	1/4/2016	10.12	
10.10+	Employment Offer Letter, dated June 12, 2014, between the Registrant and Katrine S. Bosley	S-1	333-208856	1/4/2016	10.13	
10.11+	Amended and Restated Offer of Employment, dated July 24, 2016, between the Registrant and Charles Albright, Ph.D.					X
10.12+	Employment Offer Letter, dated July 19, 2016, between the Registrant and Gerald Cox, M.D., Ph.D.					X
10.13+	Inducement Stock Option Agreement, dated October 5, 2016, between the Registrant and Gerald F. Cox, M.D., Ph.D.	S-8	333-214556	11/10/2016	99.1	
10.14	Form of Director Indemnification Agreement between the Registrant and each of Kevin Bitterman, Ph.D., Alexis Borisy, Douglas G. Cole, M.D., and Boris Nikolic, M.D. during the year ended December 31, 2015	S-1	333-208856	1/4/2016	10.16	
10.15†	License Agreement, dated August 29, 2014, between the Registrant and The General Hospital Corporation, d/b/a Massachusetts General Hospital	S-1	333-208856	1/4/2016	10.19	
10.16	First Amendment to Exclusive Patent License Agreement, dated as of June 29, 2015, by and between the Registrant and the General Hospital Corporation, d/b/a Massachusetts General Hospital					X

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10.17†	Second Amendment to Exclusive Patent License Agreement, dated as of November 17, 2016, by and between the Registrant and the General Hospital Corporation, d/b/a/ Massachusetts General Hospital	8-K	001-37687	1/23/2017	99.4	
10.18†	License Agreement, dated October 10, 2014, between the Registrant and Duke University	S-1	333-208856	1/4/2016	10.20	
10.19	Letter Agreement, dated October 9, 2015, between the Registrant and Duke University	S-1	333-208856	1/4/2016	10.21	
10.20†	Amended and Restated Cas9-I License Agreement, dated December 16, 2016, among the Registrant, the President and Fellows of Harvard College, and the Broad Institute, Inc.	8-K	001-37687	1/23/2017	99.2	
10.21†	License and Collaboration Agreement, dated May 26, 2015, between the Registrant and Juno Therapeutics, Inc.	S-1	333-208856	1/4/2016	10.23	
10.22+	Summary of Director Compensation Program	S-1	333-208856	1/4/2016	10.24	
10.23+	2015 Employee Stock Purchase Plan	S-1	333-208856	1/4/2016	10.25	
10.24+	Severance Benefits Plan	S-1	333-208856	1/4/2016	10.27	
10.25	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers	S-1	333-208856	1/4/2016	10.28	
10.26	Lease Agreement, dated February 12, 2016, between Registrant and ARE-MA Region No. 55 Exchange Holding LLC	8-K	001-37687	2/19/2016	99.1	
10.27†	Exclusive Patent License Agreement, dated as of August 2, 2016, by and between the Registrant and The General Hospital Corporation, d/b/a Massachusetts General Hospital	10-Q	001-37687	11/9/2016	10.1	
10.28†	Cpfl License Agreement, dated as of December 16, 2016, by and between the Registrant and The Broad Institute, Inc.	8-K	001-37687	1/23/2017	99.1	
10.29†	Cas9-II License Agreement, dated as of December 16, 2016, by and between the Registrant and The Broad Institute, Inc.	8-K	001-37687	1/23/2017	99.3	
21.1	Subsidiaries of the Registrant	10-K	001-37687	3/30/2016	21.1	
23.1	Consent of Ernst & Young					X
31.1	Rule 13a-14(a) Certification of Principal Executive Officer					X
31.2	Rule 13a-14(a) Certification of Principal Financial Officer					X
32.1	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. §1350					X
101.INS	XBRL Instance Document					X
101.SCH	XBRL Taxonomy Extension Schema Document					X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					X

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- † Confidential treatment has been granted as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.
- †† Confidential treatment has been requested as to certain portions, which portions in each case have been omitted and separately filed with the Securities and Exchange Commission.
- + Management contract or compensatory plan or arrangement.





July 24, 2016

Charles F. Albright, Ph.D.

Re: Offer of Employment

Dear Charlie,

On behalf of Editas Medicine, Inc. (the "Company"), I am pleased to offer you employment with the Company. The purpose of this letter is to set forth the terms of your employment with the Company, should you accept our offer.

I am pleased to offer you the position of Chief Scientific Officer, reporting to the Chief Executive Officer. Your base salary will be at the rate of \$15,625.00 per semi-monthly pay period (equivalent to an annualized base salary of \$375,000.00). You will be employed on a fulltime basis.

Additionally, you will be eligible to receive an annual performance bonus, targeted at 35% of your annual base salary, to be determined based on the achievement of your individual goals and the Company's goals during the applicable fiscal year, and on a pro-rated basis. Such bonus shall be subject to the approval of the Company's Board of Directors (or a committee thereof).

You must be an active employee of the Company on the date any bonus is distributed in order to be eligible for and to earn a bonus award, as it also serves as an incentive to remain employed by the Company, provided that the Company will award and pay any bonus for the prior calendar year before March 15<sup>th</sup> of the next succeeding calendar year.

Your effective date of hire as an employee (the "Start Date") is to be mutually agreed upon by you and the Company, but not later than September 4, 2016.

Subject to approval of the Company's Board of Directors, the Company will grant you a stock option to purchase an aggregate of 225,000 shares of the Company's common stock (the "Option") at an exercise or purchase price equal to the fair market value of the Company's common stock on the date of grant. The Option will vest over four (4) years at the rate of 25% on the first anniversary of the commencement date of your employment, and an additional 2.0833% of the original number of shares at the end of each successive month following the first anniversary of the vesting commencement date until the fourth anniversary of the vesting commencement date. The Option grant will be brought to the Board of Directors for approval after you begin employment with the Company. The Option will be evidenced in writing by and subject to the terms of the Company's 2015 Stock Incentive Plan (or such other plan, including

*Confidential*

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an inducement plan or agreement, under which such option is granted) and a stock option agreement provided by the Company.

You will be eligible to participate in the Company's Severance Benefits Plan, a copy of which is available at [https://www.sec.gov/Archives/edgar/data/1650664/00010474691600953/4a2226902zex-10\\_27.htm](https://www.sec.gov/Archives/edgar/data/1650664/00010474691600953/4a2226902zex-10_27.htm), at the level of Other C-Level Officer (as defined in the Company's Severance Benefits Plan). Your eligibility under the Severance Benefits Plan is subject to the terms and conditions thereof.

You will be eligible to participate in the Company's Medical and Dental Insurance Programs, as well as all other Company benefits, provided you are eligible under (and subject to all provisions of) the plan documents governing those programs. The benefit programs made available by the Company, and the rules, terms and conditions for participation in such benefit plans, may be changed by the Company at any time, in its sole discretion or as otherwise required by law, without advance notice.

You will be eligible for a maximum of four weeks of vacation per calendar year to be taken at such times as may be approved by the Company. The number of vacation days for which you are eligible shall accrue at the rate of 1.67 days per month that you are employed during such calendar year. Additionally, you will receive 1 personal day and 11 paid holidays annually, in accordance with the Company holiday schedule.

It is understood that you are an "at-will" employee. You are not being offered employment for a definite period of time or pursuant to an employment contract, and either you or the Company may terminate the employment relationship at any time and for any reason, with or without cause or prior notice and without additional compensation to you.

Your normal place of work will be at the offices of the Company in Cambridge, Massachusetts. Enclosed for your review is a Non-Solicitation, Non-Competition, Confidentiality and Assignment Agreement (the "Agreement"). This offer of employment is conditioned on your willingness to sign and abide by the terms of the Agreement. You will be expected to sign the Agreement on or prior to your Start Date.

In making this offer, the Company understands, based on representations made by you, that you are not under any obligation to any former employer or any person or entity which would prevent, limit, or impair in any way your acceptance of this offer or employment or the performance by you of your duties as an employee of the Company.

In accepting this offer you represent and warrant the foregoing to be true and correct and that in connection with providing services to the Company you will not (i) use any confidential and/or proprietary information of any third party, including, without limitation, any former employer, and (ii) bring any biological or other materials to the Company.

The Immigration Reform and Control Act requires employers to verify the employment eligibility and identity of new employees. You will be required to complete a Form I-9 which will be provided to you before the Start Date. Please bring the appropriate documents listed on

that form with you when you report for work. We will not be able to employ you if you fail to comply with this requirement.

This letter agreement and the Agreement referenced above constitute the complete agreement between you and the Company, contain all of the terms of your employment with the Company and supersede any prior agreements, representations or understandings (formal or informal, whether written, oral or implied) between you and the Company. This letter agreement may not be amended or modified except by an express written agreement signed by both you and a duly authorized officer of the Company, although your job duties, title, reporting relationship, compensation and benefits may change from time to time in the Company's sole discretion and provided that the "at-will" nature of your employment may only be changed by a written agreement signed by you and the Chief Executive Officer, which expressly states the intention to modify the at-will nature of your employment. Nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company, except to the extent you are eligible for post-employment benefits under the Severance Benefit Plan.

As an employee of the Company, you will be required to familiarize yourself and comply with all Company policies and procedures. Violations of the Company's policies may lead to immediate termination of your employment. Further, the Company's premises, including all workspaces, furniture, documents and other tangible materials, together with all information technology resources of the Company (including computers, portable devices, data and other electronic files (whether in hard copy or electronic form), and all internet and email communications) are subject to oversight and inspection by the Company at any time. Company employees shall have no expectation of privacy with regard to any Company premises, materials, resources or information.

Please indicate your acceptance of this offer by signing and returning the enclosed copy of this letter no later than August 1, 2016. You may indicate your acceptance of this offer by signing on the appropriate space below and returning a signed, scanned copy along with the other necessary agreements referenced in this letter to Katrine Bosley at [ksb@editasmed.com](mailto:ksb@editasmed.com) or returning by mail to Editas Medicine, Inc., 300 Third Street, Cambridge, MA 02142, Attention: Katrine Bosley. This offer will remain open until 5:00p.m. on August 1, 2016.

Please know that we are truly enthused at the prospect of you becoming part of the Editas team and at your leadership helping to build what we hope will be an exceptional organization, one that is both a scientific pioneer and that delivers transformative medicines to many, many patients. We believe that you will be a fundamental part of turning that aspiration into reality.

Very truly yours,

/s/ Katrine Bosley

\_\_\_\_\_  
Katrine Bosley  
Chief Executive Officer  
Editas Medicine, Inc.

Accepted and Agreed:

/s/ Charles F. Albright  
Charles F. Albright, Ph.D.

July 26, 2016  
Date

*Confidential*



July 19, 2016

Gerald F. Cox, M.D., Ph.D.

Re: Offer of Employment

Dear Gerry,

On behalf of Editas Medicine, Inc. (the "Company"), I am pleased to offer you employment with the Company. The purpose of this letter is to set forth the terms of your employment with the Company, should you accept our offer.

I am pleased to offer you the position of Chief Medical Officer at the Company, reporting to the Chief Executive Officer.

Your base salary will be at the rate of \$16,666.67 per semi-monthly pay period (equivalent to an annualized base salary of \$400,000.00). You will be employed on a full-time basis. Following commencement of your employment with the Company, you will be entitled to continue your ongoing work at Boston Children's Hospital on a schedule and frequency consistent with your current schedule (which is generally 0.5 days per week), provided that such activity does not interfere or conflict with your obligations to the Company (as reasonably determined by the Board of Directors of the Company).

Additionally, you will be eligible to receive an annual performance bonus, targeted at 35% of your annual base salary, to be determined based on the achievement of your individual goals and the Company's goals during the applicable fiscal year, and on a pro-rated basis. Such bonus shall be subject to the approval of the Company's Board of Directors (or a committee thereof).

You must be an active employee of the Company on the date any bonus is distributed in order to be eligible for and to earn a bonus award, as it also serves as an incentive to remain employed by the Company, provided that the Company will award and pay any bonus for the prior calendar year before March 15th of the next succeeding calendar year. Your effective date of hire as an employee (the "Start Date") is to be mutually agreed upon by you and the Company, but not later than October 3, 2016.

Subject to approval of the Company's Board of Directors, the Company will grant you a stock option to purchase an aggregate of 225,000 shares of the Company's common stock (the "Option") at an exercise or purchase price equal to the fair market value of the Company's common stock on the date of grant. The Option will vest over four (4) years at the rate of 25% on the first anniversary of the

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commencement date of your employment, and an additional 2.0833% of the original number of shares at the end of each successive month following the first anniversary of the vesting commencement date until the fourth anniversary of the commencement date of your employment. The Option grant will be brought to the Board of Directors for approval after you begin employment with the Company. The Option will be evidenced in writing by, and subject to the terms of the 2015 Stock Incentive Plan (or such other plan, including an inducement plan or agreement, under which such option is granted) and a stock option agreement provided by the Company.

You will be eligible to participate in the Company's Severance Benefits Plan, a copy of which is available at [https://www.sec.gov/Archives/edgar/data/1650664/000104746916009534/a2226902zex\\_10\\_27.htm](https://www.sec.gov/Archives/edgar/data/1650664/000104746916009534/a2226902zex_10_27.htm), at the Chief Medical Officer level. Your eligibility under the Severance Benefits Plan is subject to the terms and conditions thereof.

You will be eligible to participate in the Company's Medical and Dental Insurance Programs, as well as all other Company benefits, provided you are eligible under (and subject to all provisions of) the plan documents governing those programs. The benefit programs made available by the Company, and the rules, terms and conditions for participation in such benefit plans, may be changed by the Company at any time, in its sole discretion or as otherwise required by law, without advance notice.

You will be eligible for a maximum of four weeks of vacation per calendar year to be taken at such times as may be approved by the Company. The number of vacation days for which you are eligible shall accrue at the rate of 1.67 days per month that you are employed during such calendar year. Additionally, you will receive 1 personal day and 11 paid holidays annually, in accordance with the Company holiday schedule.

It is understood that you are an "at-will" employee. You are not being offered employment for a definite period of time or pursuant to an employment contract, and either you or the Company may terminate the employment relationship at any time and for any reason, with or without cause or prior notice and without additional compensation to you.

Your normal place of work will be at the offices of the Company in Cambridge, Massachusetts. Enclosed for your review is a Non-Solicitation, Non-Competition, Confidentiality and Assignment Agreement (the "Agreement"). This offer of employment is conditioned on your willingness to sign and abide by the terms of the Agreement. You will be expected to sign the Agreement on or prior to your Start Date.

In making this offer, the Company understands, based on representations made by you, that you are not under any obligation to any former employer or any person or entity which would prevent, limit, or impair in any way your acceptance of this offer or employment or the performance by you of your duties as an employee of the Company. In accepting this offer you represent and warrant the foregoing to be true and correct and that in connection with providing services to the Company you will not (i) use any confidential and/or proprietary information of any third party, including, without limitation, any former employer, and (ii) bring any biological or other materials to the Company.

The Immigration Reform and Control Act requires employers to verify the employment eligibility and identity of new employees. You will be required to complete a Form I-9 which

will be provided to you before the Start Date. Please bring the appropriate documents listed on that form with you when you report for work. We will not be able to employ you if you fail to comply with this requirement.

This letter agreement and the Agreement referenced above constitute the complete agreement between you and the Company, contain all of the terms of your employment with the Company and supersede any prior agreements, representations or understandings (formal or informal, whether written, oral or implied) between you and the Company.

This letter agreement may not be amended or modified except by an express written agreement signed by both you and a duly authorized officer of the Company, although your job duties, title, reporting relationship, compensation and benefits may change from time to time in the Company's sole discretion and provided that the "at-will" nature of your employment may only be changed by a written agreement signed by you and the Chief Executive Officer, which expressly states the intention to modify the at-will nature of your employment. Nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company, except to the extent you are eligible for post-employment benefits under the Severance Benefit Plan.

As an employee of the Company, you will be required to familiarize yourself and comply with all Company policies and procedures. Violations of the Company's policies may lead to immediate termination of your employment. Further, the Company's premises, including all workspaces, furniture, documents and other tangible materials, together with all information technology resources of the Company (including computers, portable devices, data and other electronic files (whether in hard copy or electronic form), and all internet and email communications) are subject to oversight and inspection by the Company at any time. Company employees shall have no expectation of privacy with regard to any Company premises, materials, resources or information.

Please indicate your acceptance of this offer by signing and returning the enclosed copy of this letter no later than July 20, 2016. You may indicate your acceptance of this offer by signing on the appropriate space below and returning a signed, scanned copy along with the other necessary agreements referenced in this letter to Katrine Bosley at [ksb@editasmed.com](mailto:ksb@editasmed.com) or returning by mail to Editas Medicine, Inc., 300 Third Street, Cambridge, MA 02142, Attention: Katrine Bosley. This offer will remain open until 5:00 p.m. on the 5th business day after your receipt of this offer.

Please know that we are truly enthused at the prospect of you becoming part of the Editas team and at your leadership helping to build what we hope will be an exceptional organization, one that is both a scientific pioneer and that delivers transformative medicines to many, many patients. We believe that you will be a fundamental part of turning that aspiration into reality.

Very truly yours,

/s/ Katrine Bosley

Katrine Bosley  
Chief Executive Officer  
Editas Medicine, Inc.

Accepted and Agreed:

/s/ Gerald F. Cox

Gerald F. Cox, M.D., PhD

19 July 2016

Date

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**FIRST AMENDMENT  
TO EXCLUSIVE PATENT LICENSE AGREEMENT**

**MGH Agreement No: A221317**

This First Amendment (“First Amendment”) to the Exclusive Patent License Agreement by and between Editas Medicine, Inc. (“Company”) and The General Hospital Corporation d/b/a Massachusetts General Hospital (“Hospital”) dated as of August 29, 2014 (“Agreement”) is made as of the 29<sup>th</sup> day of June, 2015 (the “First Amendment Effective Date”). Capitalized terms used in this First Amendment that are not otherwise defined herein shall have the same meanings as such terms are given in the Agreement. Each reference to a Section herein is a reference to such Section of the Agreement.

**WHEREAS**, the Parties wish to amend the Agreement to clarify the rights and obligations of the Parties with respect Confidential Information (as defined in Appendix E attached to the Agreement);

**NOW THEREFORE**, in consideration of the premises and mutual covenants contained in this First Amendment, the Parties agree as follows:

1. A new Section 12.14 is hereby added to Agreement, to read in its entirety as follows:

“12.14 Confidentiality.

- (a) **Appendix E** attached hereto is incorporated by reference into Agreement.
- (b) All reports and other information disclosed by Company to Hospital pursuant to Sections 2.3, 3, 4 and 5, and any information obtained by Hospital pursuant to any audit conducted under Section 5.5, shall be included in the “Confidential Information” of Company (as such term is defined and used in **Appendix E**).
- (c) The terms and conditions of Agreement shall be the “Confidential Information” of each of Company and Hospital.
- (d) Notwithstanding anything in **Appendix E** to the contrary, Company may disclose the Confidential Information of the Hospital (i) to actual and *bona fide* potential investors, lenders and acquirors/acquirees, merger partners, other financial or commercial partners to the extent necessary in connection with a proposed equity or debt financing of Company, or a proposed acquisition or business combination, or to actual and *bona fide* potential sublicensees, so long as such recipients are bound in writing to maintain the confidentiality of such information in accordance with the terms of Agreement and/or (ii) to the extent required under the rules or regulations of the U.S. Securities and Exchange Commission, or any similar regulatory agency in any country other than the United States, or of any stock exchange, including Nasdaq; provided that, to the extent

practicable, Company promptly notifies Hospital prior to such required disclosure, discloses such information only to the extent so required and cooperates reasonably with Hospital's efforts to contest or limit the scope of such disclosure."

2. Except as expressly amended hereby, the terms and conditions of Agreement shall remain unchanged and in full force and effect. In the event of any conflict between the terms of this First Amendment and the terms of Agreement, the terms of this First Amendment shall govern. This First Amendment shall be effective as of the First Amendment Effective Date.

*[Signature page follows]*

IN WITNESS WHEREOF, the Parties have caused this First Amendment to be executed by their duly authorized representatives as of the First Amendment Effective Date.

**EDITAS MEDICINE, INC.**

By: /s/ Katrine S. Bosley

Name: Katrine S. Bosley

Title: President and CEO

**GENERAL HOSPITAL CORPORATION**

By: /s/ Daniel Castro

Name: Daniel Castro

Director, Business Strategy  
And Licensing, Innovation  
Title: Partners HealthCare

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the Registration Statement (Form S-8) pertaining to the 2013 Stock Incentive Plan, the 2015 Stock Incentive Plan and the 2015 Employee Stock Purchase Plan of Editas Medicine, Inc. of our report dated March 3, 2017, with respect to the consolidated financial statements of Editas Medicine, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2016.

/s/ Ernst & Young LLP

Boston, Massachusetts  
March 3, 2017

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## CERTIFICATIONS

I, Katrine S. Bosley, certify that:

1. I have reviewed this Annual Report on Form 10-K of Editas Medicine, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting.
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 3, 2017

By: /s/ Katrine S. Bosley  
Katrine S. Bosley  
Chief Executive Officer  
(Principal Executive Officer)

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## CERTIFICATIONS

I, Andrew A.F. Hack, certify that:

1. I have reviewed this Annual Report on Form 10-K of Editas Medicine, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting.
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 3, 2017

By: /s/ Andrew A. F. Hack  
Andrew A. F. Hack, M.D., Ph.D.  
Chief Financial Officer  
(Principal Financial Officer)

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**CERTIFICATIONS OF CEO AND CFO PURSUANT TO 18 U.S.C. SECTION 1350,  
AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with this Annual Report on Form 10-K of Editas Medicine, Inc. (the "Company") for the year ended December 31, 2016, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. (section) 1350, as adopted pursuant to (section) 906 of the Sarbanes-Oxley Act of 2002, that to the best of her or his knowledge:

- (1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 3, 2017

By: /s/ Katrine S. Bosley  
Katrine S. Bosley  
President and Chief Executive Officer

By: /s/ Andrew A.F. Hack  
Andrew A.F. Hack, M.D., Ph.D.  
Chief Financial Officer

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