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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2017

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from _____ to _____

Commission File Number 001-37687

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

Delaware **(State or other jurisdiction of incorporation or organization)**	**46-4097528** **(I.R.S. Employer Identification No.)**
11 Hurley Street **Cambridge, Massachusetts** **(Address of principal executive offices)**	**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	**Name of each exchange on which registered**
Common Stock, $0.0001 par value per share	**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 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

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

As of June 30, 2017, 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 $502,961,068, based upon the closing price of the registrant's Common Stock on June 30, 2017.

The number of shares of the registrant's Common Stock outstanding as of February 28, 2018 was 46,884,857.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2018 Annual Meeting of Stockholders to be filed pursuant to Regulation 14A within 120 days of the end of the registrant's fiscal year ended December 31, 2017 are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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 developing transformative genomic medicines with the aim to treat a broad range of serious diseases. The promise of genomic medicines is supported by the advancing knowledge of the human genome, and harnessing the progress in technologies for cell therapy, gene therapy, and, most recently, genome editing. We believe this progress sets the stage for us to create unprecedented medicines with the potential to have a durable benefit for patients. At Editas Medicine, our core capability in genome editing uses the technology known as CRISPR (clustered, regularly interspaced, short palindromic repeats) with which we can create molecules that efficiently and specifically edit DNA. Our mission is to translate the promise of this science into a broad class of medicines to help people living with serious diseases around the world.

We have developed a proprietary genome editing platform based on CRISPR technology and we continue to expand its capabilities. 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 and guide RNA engineering, delivery, control and specificity, and directed editing. These interrelated 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.

We believe we are the only human genome editing company with a platform that includes CRISPR/Cas9, CRISPR/Cpf1, and engineered forms of both of these CRISPR systems. Because of the broad nature of this platform, we believe we can create genome editing molecules for almost any site in the human genome. Each of our product candidates derives from our platform, and we plan to continue to use our platform to create and advance a broad range of experimental medicines for both genetically defined and genetically treatable diseases.

Our initial product development strategy is to primarily target genetically defined diseases with a focus on debilitating illnesses where there are poor or no approved treatments and where the genetic basis of disease is well understood. 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. While our discovery efforts have ranged across several different diseases and therapeutic areas, the two areas where our programs are more mature are ocular diseases and engineered cell medicines.

In ocular diseases, our most advanced program is designed to address Leber Congenital Amaurosis type 10 ("LCA10"), which is a specific genetic form of vision loss that leads to blindness in childhood. LCA10 has no approved therapies in either the United States or European Union, and we are aware of only one potential treatment in clinical trials in the United States and Europe. LCA10 patients have a mutation in the CEP290 gene that causes the disease. We have demonstrated that our lead product candidate, EDIT-101, can achieve high levels of editing of the CEP290 gene in human retinal tissue that has been explanted and maintained *in vitro* and in the retinas of non-human primates *in vivo*. We have initiated a clinical natural history study to evaluate the clinical course and characteristics of LCA10 more extensively, and we aim to file an investigational new drug application ("IND") by mid-2018 for EDIT-101. We believe results to date in LCA10 validate our platform technology, including its potential application to other ocular diseases, such as Usher Syndrome 2A ("USH2A") and recurrent ocular Herpes Simplex Virus 1 ("HSV-1") infection, as well as diseases of other organs and tissues.

In March 2017 we entered into a strategic alliance and option agreement with Allergan Pharmaceuticals International Limited ("Allergan"), which we believe has the potential to expand and enhance our research and development efforts for ocular diseases. Under this agreement, Allergan received exclusive access and the option to license up to five of our genome editing ocular programs, including our lead program for LCA10, and will be responsible for development and commercialization of any program with respect to which it exercises its option. For

LCA10 and one additional program, we retain the option to co-develop and co-commercialize products in the United States. We received an upfront payment of $90.0 million and have the potential to receive greater than $1.0 billion in contingent milestone payments, as well as high single-digit royalties. With Allergan, we aim to advance a broad portfolio of first-in-class genome editing medicines to treat serious diseases of the eye.

In addition to developing medicines for ocular diseases, the development of engineered cell medicines is a core part of our research effort and product pipeline. We believe that advances in genome editing will both improve the characteristics of current cellular medicines and also expand the universe of cellular medicines that can be created. To this end, we have developed capabilities to efficiently and specifically edit T cells and hematopoietic stem cells, which we believe have the potential to lead to best-in-class medicines for cancer and hemoglobinopathies. More broadly, we believe that our editing capabilities can be applied to many additional cell types.

In May 2015 we established a collaboration with Juno Therapeutics, Inc. ("Juno Therapeutics") to develop engineered T cell medicines for cancer. These therapies have the potential to substantially advance the field of cancer immunotherapy and expand the range of cancers that can be treated with engineered T cells. Under the collaboration, we received an upfront payment of $25.0 million, and we have received two milestone payments totaling $5.0 million related to technical progress in research programs under the collaboration. We also have the potential to receive approximately $700.0 million in aggregate in potential milestone payments, as well as tiered royalties. In addition, we are eligible to receive research support of up to $22.0 million over the initial five year research term, subject to adjustment in accordance with the terms of the collaboration.

We are also developing multiple gene editing approaches to treating hemoglobinopathies. These programs take advantage of our genome editing capabilities in hematopoietic stem cells ("HSCs"), which include two distinct genome editing approaches at the hemoglobin gene locus. We believe one or both of these approaches has the potential to effectively and durably treat sickle cell disease and beta thalassemia.

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, Culture, and Team

Our values are the critical foundation upon which we have built our organization. They reflect how we think about the patients we aspire to help, how we operate as a company, and who we hire. These values are:

- **C**ommunity: One Team—Many Voices—Shared Mission
- **R**esilience: Respect—Grow—Learn
- **I**ngenuity: Be Bold—Answer Unknowns—Create Therapies
- **S**cience: Impeccable—Rigorous—Meaningful
- **P**assion: Love It—Do It—Own It
- **R**evolution: Discover—Translate—Cure

We believe that our values, culture, and team 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 team's substantial experience in translating groundbreaking scientific platforms into therapeutic products and product candidates in many different diseases. This experience extends to our board of directors, which is composed of people with deep experience in guiding biotechnology companies through rapid growth and the development of complex, breakthrough science.

Our Strategy and Long Term Goals

We aim to transform the treatment of a broad range of serious diseases by building an integrated genomic medicine company. Key elements of our strategy are to:

- build the preeminent genomic medicine company;
- advance therapeutic programs rapidly and rigorously to address patients' needs;
- perfect the tools to edit DNA;
- accelerate the translational science of genome editing;
- collaborate to realize the full potential of genome editing to create medicines; and
- commercialize products to bring new medicines to patients.

As part of our long term strategy, we have developed and articulated goals for our pipeline of experimental medicines and our company that we are working to achieve by the end of 2022. These goals, which we call "EM22", include having at least three experimental medicines in early stage clinical trials and at least two additional experimental medicines in or ready for late stage clinical trials. In addition, we aim to have a pipeline characterized by potential best-in-class medicines and to be a company with the leading genome editing platform and organizational culture.

Our Core Capability — 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 blueprint for cellular structure and function. Small changes, or mutations, can occur in the sequence of 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. 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. 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 therapy and genome editing. Each approach seeks to address genetically defined diseases at the level of DNA.

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*. In general, 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. Genome editing typically takes advantage of naturally occurring DNA repair mechanisms, including non-homologous end joining ("NHEJ") and homology directed repair ("HDR"), to achieve its desired therapeutic outcome. Edits that are repaired by NHEJ typically disrupt a gene or eliminate a disease causing mutation. Edits that are repaired by HDR, including targeted insertion, aim to correct or replace aberrant DNA sequences. 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.

Advantages of CRISPR for Genome Editing

CRISPR technology uses a protein-RNA complex composed of a type of enzyme, referred to as a DNA endonuclease, bound to an RNA molecule, referred to as a guide RNA, that has been designed to recognize a particular DNA sequence. A DNA endonuclease is an enzyme that cleaves DNA. This combination of a DNA endonuclease and a guide RNA only bind and cut DNA when two criteria are met: first, the protein recognizes a short DNA specific to the enzyme called the protospacer adjacent motif ("PAM"), and second, the appropriate portion of the guide RNA matches the adjacent DNA sequence. The PAM sequence that is recognized by the DNA endonuclease creates a second layer of recognition in addition to the guide RNA. 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 a 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 ("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 along with the same endonuclease, 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 control exposure to the editing machinery. To address more than one target, other genome editing technologies require the engineering, characterization, manufacture, and delivery of distinct nuclease proteins for each target.

- *Ability to achieve a range of different types of edits.* The inherent differences in Cas9 and Cpf1 and the availability of different engineered variants of both enzymes allow for different types of cuts for genome editing. We are able to make a blunt cut, cut either strand of the DNA, or create overhangs of differing length. 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.

Our Genome Editing Platform

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

- creating a comprehensive toolbox for robust and selective genome engineering;

- providing efficient and targeted delivery to any tissue or cell;
- effecting spatial and temporal control of gene editing and specificity; and
- orchestrating the cellular response to ensure accurate and precise genome editing.

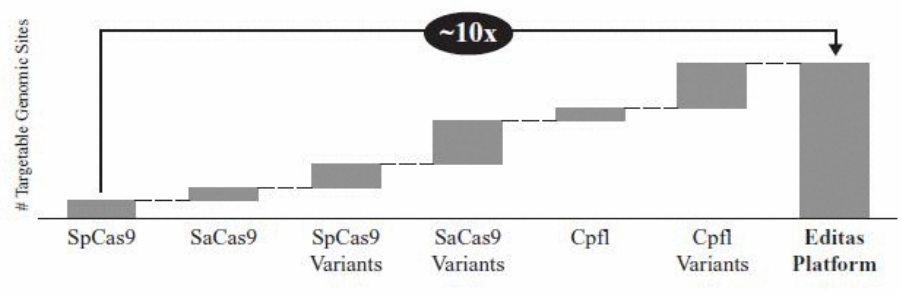
We believe that the developments we have made in our genome editing platform position us to be able to identify and develop innovative genome editing therapies targeting a wide variety of diseases. All of our programs to develop medicines leverage aspects of this platform while also providing insights 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 and Guide RNA 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 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 and characterize 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 have higher fidelity than naturally occurring Cas9. We believe that further developing our nuclease and guide RNA 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* ("*S. aureus*" or "SaCas9") is significantly smaller than that from *Streptococcus pyogenes* ("*S. pyogenes*" or "SpCas9") (3,159 vs. 4,104 base pairs), and this is important when working with adeno-associated virus ("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. Thus, while the *S. pyogenes* Cas9 can target approximately 1 in 10 bases in the human genome, we have the potential to hit over 95% of all bases due to the wide range of endonucleases at our disposal.

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.

Of critical importance in determining the activity and specificity of an endonuclease-guide RNA complex is understanding the quality and composition of the guide RNA. The ability to understand the quality and composition of the guide RNA will be an essential component to developing product candidates that have the potential to be safe and efficacious medicines. We have developed significant analytical and synthetic capabilities as a result of acquiring assets and capabilities of i2 Pharmaceuticals, Inc. and certain of its affiliated companies in January 2018. In addition to state of the art mass spectrometry and sequencing methodologies to understand the absolute composition of our guide RNAs, we have developed two-step synthesis methods which results in guide RNAs which we believe are significantly superior to those generated by other approaches. This method allows us to independently synthesize and purify guide RNAs in multiple parts and covalently couple them using a proprietary catalyst-free chemistry. These covalently coupled, dual guide RNAs retain the advantages afforded by a single guide RNA and we believe are of higher quality than a guide RNA made by a single synthesis reaction. We believe this method will lead to higher quality genome editing medicines.

Delivery

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. 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 AAVs, lipid nanoparticles ("LNPs"), and the use of electroporation. For example, 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 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. In addition, 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 greater than 90% *ex vivo* editing on multiple genetic targets simultaneously in human T cells and greater than 75% *ex vivo* editing in hematopoietic stem cells using ribonucleoprotein complexes, which consist of the Cas9 or Cpf1 endonuclease complexed with its guide RNA. These results are consistent across multiple cell donors and multiple target genes.

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.* In order to design highly selective guide RNAs, 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 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 so that we can select for advancement those molecules with no off-target activity in these assays.

- *Create validated assay panels composed of potential off-target sites identified by both computational approaches and other unbiased methods.* These verification assay panels, or targeted resequencing assay, will then be applied to *in vitro* and *in vivo* experimental systems to confirm specificity as we advance to the clinic. Included in these assay panels are genome detection methods that allow detection of multiple editing events in a single reaction. Our proprietary Uni-Directional Targeted Sequencing method ("UDiTaS") is a simple, efficient way to simultaneously measure small and large editing events at single nucleotide resolution and provide accurate quantification of these events.

To optimize the specificity of our product candidates, there are a number of different aspects of the product configuration that we customize in addition to the sequence and quality of the guide RNA, including 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. For example, to reduce the potential 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 expected to have been completed.

Directed Editing

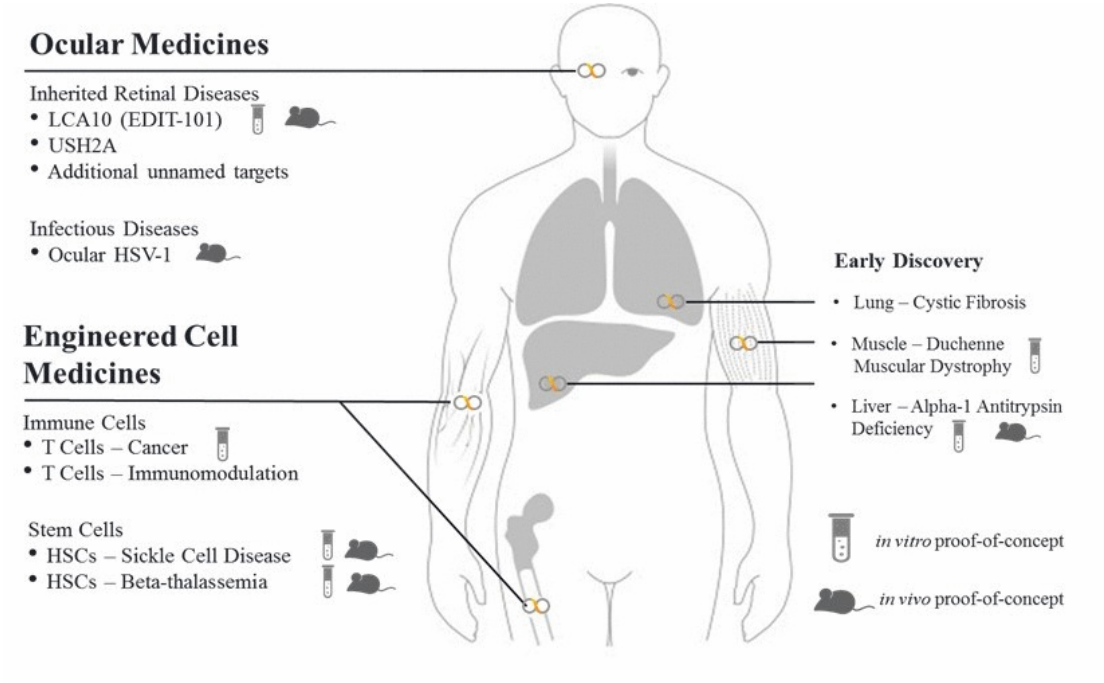
There are different mechanisms that a cell can use to repair cuts in DNA. Each mechanism results in different kinds of genetic changes. We are developing approaches to selectively harness specific DNA repair mechanisms to be able to drive the appropriate type of repair for a given disease. The ability 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.

We have achieved significant levels of DNA template directed genetic change in *ex vivo* edited primary human T cells and hematopoietic stem cells. Using long single stranded DNA template molecules, we have achieved greater than 40% directed editing. Using vial donor templates, we have achieved greater than 70% targeted insertion at specific genomic locations. We believe that these advancements will enable us to create medicines that may be superior to traditional gene therapy.

Our Genomic Medicine Programs

We have initiated a diversified range of research programs across multiple therapeutic areas. Our initial product development strategy is to primarily target genetically defined diseases with a focus on debilitating illnesses where there

are poor or no approved treatments and where the genetic basis of disease is well understood. While our discovery efforts have ranged across several different diseases and therapeutic areas, the two areas where programs are more mature are ocular diseases and engineered cell medicines. 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 with either genetically defined or genetically treatable diseases. A summary of our experimental medicines under development is presented in the following graphic:



Eye Diseases

We have granted Allergan an exclusive option to exclusively license from us up to five collaboration development programs for the treatment of ocular disorders, including our LCA10 program, subject to our right to elect to participate in a profit-sharing arrangement with Allergan in the United States with respect to our LCA10 program and up to one other collaboration development program. See "*Our Collaboration and Licensing Strategy*" below for more information.

Leber Congenital Amaurosis 10

Leber Congenital Amaurosis ("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 to a lack of functional photoreceptor cells. The most common form of the disease is LCA10, a monogenic disorder that 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 a deficiency of functional CEP290 protein. Decreased CEP290 protein leads to loss of photoreceptor function and cells over time, which leads to blindness.

We are developing a genome editing therapeutic for LCA10 that uses an AAV5 vector to deliver the DNA encoding Cas9 and two guide RNAs to photoreceptor cells in the eye. Our product candidate is called EDIT-101 and it is designed to eliminate the A to G nucleotide change in a non-coding region, or intron, of the CEP290 gene by cutting out that nucleotide and surrounding DNA. We believe this genome editing approach has the potential to restore normal protein expression and function of the remaining photoreceptor cells, which could arrest or improve the further loss of vision in LCA patients.

We have tested combinations of Cas9 and guide RNA pairs *in vitro* in cells that were obtained from patients with the CEP290 mutation to determine whether they could successfully edit the mutation and lead to correctly spliced messenger RNA ("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. These studies also demonstrated that the edit restored significant levels of normal mRNA and lowered the levels of mutant mRNA, as compared to controls of untreated patient cells. This restoration of normal mRNA expression suggests that we successfully edited the LCA10 gene defect in these cells.

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

Certain clinical research studies estimated that retention of 10% of photoreceptors can impart meaningful vision in humans. Based on these studies, we have prespecified a therapeutic target of 10% productive editing of photoreceptors with the assumption that each productively edited photoreceptor will be fully functional.

To investigate genome editing *in vivo*, we conducted studies in nonhuman primates using subretinal injection of an AAV5 expressing Cas9 and nonhuman primate specific guide RNAs. After either six or 13 weeks, animals were euthanized and retinal tissue from the injected region was removed for analysis. These studies showed that AAV genomes and Cas9 expression were limited to photoreceptors. In addition, we estimate that 12-22% and 50% of CEP-290 alleles were productively edited at six weeks and at 13 weeks, respectively. In these studies, productive editing is defined as the proportion of photoreceptor cells edited in a manner that we believe will restore CEP290 protein function. All of these values exceed our prespecified therapeutic target of 10% productive editing.

In addition, we developed a retinal explant system to explore the potential effectiveness EDIT-101 in human tissue. In these studies, retinas from human cadavers were dissected, placed in culture, and exposed to EDIT-101 at a low and a high dose. After 14 days or 28 days in culture, genome editing was analyzed to determine the rate of productive editing in photoreceptors. These studies showed time-dependent and dose-dependent editing that exceeded our therapeutic target at all times and doses tested, including over 50% editing after 28 days at the high dose.

To characterize editing specificity, we have applied a combination of methods to quantify the frequency of modification at the targeted DNA location and to assess the potential for modification at off-target locations in the genome. For each guide RNA included in the studies above, we measured the potential for off-target activity using multiple analytical techniques, including GUIDE-Seq, Digenome-Seq, our proprietary UDiTaS system, and bi-directional polymerase chain reaction and deep sequencing. With these techniques we have assessed the specificity of each guide RNA in certain cell culture systems and tissue types and we were able to clearly identify several guide RNAs that showed no detectable off-target activity. We believe our detailed characterization of editing specificity allows us to select guide RNA and endonuclease combinations with the highest likelihood of providing clinical benefit in patients while working to minimize potential safety risks.

Other Eye Diseases

We are also pursuing the development of therapies for eye diseases other than LCA10, including HSV-1, infections and USH2A. 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 the most common cause of USH2A.

Herpes Simplex Virus 1

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 latency, the HSV-1 DNA does not integrate into the infected individual's genome, but rather 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 developed economies with over 25,000 recurrent cases each year. Recurrent activation of HSV-1 virus causes corneal damage and scarring, which impairs the ability to see. Existing therapies have only partial benefit in preventing the 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. Our ongoing research program aims 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.

Usher Syndrome 2A

USH2A gene mutations are the most common cause of Usher syndrome, a form of retinitis pigmentosa that also includes hearing loss. 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. We believe there are approximately 14,000 USH2A patients including up to approximately 4,000 Usher syndrome patients with the mutation we aim to correct.

We have granted Allergan an exclusive option to exclusively license from us up to five collaboration development programs for the treatment of ocular disorders, including our LCA10 program, subject to our right to elect to participate in a profit-sharing arrangement with Allergan in the United States with respect to our LCA10 program and up to one other collaboration development program. See "*Our Collaboration and Licensing Strategy*" below for more information.

Engineered Cell Medicines

Collaboration with Juno Therapeutics on Engineered T Cells to Treat Cancer

Engineered T cells have shown encouraging clinical activity against multiple cancers, culminating in the recent approval of two such therapies in the United States. Because of these promising results, there is significant interest in the medical community in expanding the application of this technology across a broader range of cancers and patients. We believe that our genome editing technology has the potential to improve multiple properties of these T cell therapies. If we are successful, genome-edited engineered T cells have the potential to significantly expand the types of cancers treatable by chimeric antigen receptor ("CAR")/engineered T cell receptor ("Engineered TCR") 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 have applied our genome editing technology to multiple gene targets in order to improve the efficacy and safety of CAR/ Engineered TCR T cells directed against a range of tumor types. In addition, we are currently optimizing genome editing components and delivery methods compatible with engineered T cell manufacturing methods developed by Juno Therapeutics. We have achieved success in a number of areas within our collaboration with Juno Therapeutics and have received two milestone payments to date, totaling $5.0 million.

One important challenge in the field of T cell therapies for cancer has been to use Engineered TCRs to direct the elimination of cancers based on the presence of intracellular cancer antigens. Engineered TCRs differ from CARs in that they recognize small peptides that are generally derived from proteins that reside inside the cell. These intracellular

proteins are important potential targets for cancer immunotherapy. With Juno Therapeutics, we have demonstrated in preclinical studies that disruption of the natural T cell receptor combined with the introduction of an Engineered TCR resulted in significantly improved *in vitro* T cell function. Furthermore, the elimination of the natural T cell receptor ("TCR") has the potential to make a safer medicine as the Engineered TCR will not be able to interact with the natural TCR to create new, and potentially unwanted, functionality. We believe this innovation may broaden the therapeutic opportunity for engineered T cells.

Non-malignant Hematologic Diseases

We are developing approaches for genome editing in HSCs to support the advancement of research programs to treat non-malignant hematological diseases. For example, we are actively pursuing multiple gene editing approaches to treating hemoglobinopathies and assessing other opportunities to develop medicines for diseases where we believe gene editing of HSCs is likely to produce a therapeutic effect.

We have taken two distinct genome editing approaches at the hemoglobin locus with the aim of developing best-in-class medicines for sickle cell disease and beta thalassemia. Our first approach is focused on editing a novel site within the hemoglobin locus that we believe has the potential to create superior expression of fetal hemoglobin. Based on the observation that patients with elevated fetal hemoglobin levels have better clinical outcomes, we believe this approach could significantly benefit people with sickle cell disease. Our second genome editing approach uses CRISPR editing and targeted insertion to restore natural hemoglobin expression and eliminate the sickle cell mutation. Using this approach, we have shown in studies that we can achieve greater than 30% targeted insertion at the beta globin gene locus, the gene locus that contains the sickle cell mutation, in CD34+ human stem cells, and we believe that this may restore hemoglobin expression and eliminate the sickle cell mutation.

Early Discovery Programs

Duchenne Muscular Dystrophy

Duchenne muscular dystrophy ("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 United States Food and Drug Administration (the "FDA") has approved only two therapies for the treatment of DMD. 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.

Cystic Fibrosis

Cystic fibrosis ("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. The gene that causes CF encodes the cystic fibrosis transmembrane conductance regulator ("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. Correcting the CF mutations in lung epithelial

cells will require efficient editing of these cells and development of advanced pulmonary delivery modalities. We aim 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. ("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 caused by production of an abnormal alpha-1 antitrypsin ("A1AT") protein, leading to lung and liver disease. A1AT is one of the primary proteins made in the liver and its normal activity 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 in the liver and may cause cirrhosis. In addition, loss of A1AT activity in the lung may result in emphysema. 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 Collaborations and Licensing Strategy

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 CARs and 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.

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 (the "Exclusive 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 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 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 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 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 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, 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 ("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 we have received two milestone payments totaling $5.0 million under the collaboration for technical progress in two research programs. 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 $12.2 million as of December 31, 2017, inclusive of the $5.0 million in milestone payments. We are eligible to receive future research and regulatory milestones of approximately $160.0 million for each of the first products developed in each of the three research programs, of which we have achieved two milestone payments of $2.5 million each. We also are eligible to receive future commercial sales milestones of $75.0 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.

As of the date of this Annual Report on Form 10-K, Juno Therapeutics has been acquired by Celgene Corporation. We do not anticipate that this acquisition will have a significant impact on our collaboration with Juno Therapeutics.

Allergan Strategic Alliance and Option Agreement

In March 2017, we entered into a strategic alliance and option agreement with Allergan to discover, develop, and commercialize new gene editing medicines for a range of ocular disorders. Over a seven-year research term, Allergan will have an exclusive option to exclusively license from us up to five collaboration development programs for the treatment of ocular disorders (each, a "Collaboration Development Program"), including our LCA10 Program. We will use commercially reasonably efforts to develop at least five Collaboration Development Programs and deliver preclinical results and data meeting specified criteria with respect to each Collaboration Development Program (each, an "Option Package") to Allergan. We will generally have responsibility for the conduct of each Collaboration Development Program and sole responsibility for all development costs of each Collaboration Development Program prior to any exercise by Allergan of its option to acquire an exclusive license to such Collaboration Development Program under the terms of the agreement. If at the end of the seven-year research term we have not delivered five Collaboration Development Programs that satisfy the Option Package criteria for each such program, the research term shall automatically extend by one-year increments until such obligation is satisfied, up to three additional years (the "Research Term"). In connection with entering into this agreement, Allergan paid us a one-time up-front payment of $90.0 million. In addition, within 45 days of the acceptance by the applicable regulatory authority of our submission of an investigational new drug application with respect to the LCA10 Program, Allergan is required to pay us a one-time payment of $25.0 million, whether or not Allergan exercises its option under the agreement to acquire an exclusive license with respect to the LCA10 Program.

Upon delivery of an Option Package with respect to a Collaboration Development Program to Allergan, Allergan is entitled, for specified periods of time thereafter (each, an "Initial Option Period"), to exercise an option (an "Option") to acquire from us an exclusive (even as to us and our affiliates) world-wide right and license to our background intellectual property and our interest in the Collaboration Development Program intellectual property to

develop, commercialize, make, have made, use, offer for sale, sell, and import any gene editing therapy product that results from such Collaboration Development Program during the term of the agreement (a "Licensed Product") in any category of human diseases and conditions other than the diagnosis, treatment or prevention of any cancer in humans through the use of engineered T-cells and subject to specified other limitations. Following the exercise of an Option, Allergan will have the right to grant sublicenses subject to specified terms, under Allergan's exclusive license to our background intellectual property and our interest in the Collaboration Development Program intellectual property, to develop, commercialize, make, have made, use, offer for sale, sell, and import Licensed Products.

Upon the exercise of an Option within the Initial Option Period, Allergan is required to pay to us an option exercise fee of $15.0 million. At any time during the Initial Option Period, Allergan may also elect to extend the period of time in which it may exercise the Option to permit additional development work with respect to the Collaboration Development Program, and in connection with such extension Allergan will be required to pay us an option extension fee of $5.0 million. If, following such an extension, Allergan exercises the Option following the Initial Option Period, Allergan will be required to pay us a higher option exercise fee of $22.5 million plus specified costs incurred by us in connection with the additional development work. If Allergan does not exercise an Option within a specified option exercise period and any extension thereof, such Option will terminate.

In addition, subject to specified limitations, at the end of the Research Term, Allergan will have the right, for a specified period of time, to exercise an Option with respect to each Collaboration Development Program for which we have not yet delivered an Option Package. Upon the exercise by Allergan of any such option, Allergan is required to pay to us an option exercise fee in the low-seven digits.

Following the exercise by Allergan of an Option with respect to a Collaboration Development Program, Allergan will be responsible for the development, manufacturing and commercialization of any Licensed Products thereunder and will be required to use commercially reasonable efforts to develop, obtain regulatory approval for and commercialize at least one Licensed Product thereunder. If Allergan exercises its Option for the LCA10 Program, subject to Allergan's financial responsibility and final decision-making authority with respect to any development activities following such exercise, we will remain primarily responsible for conducting the LCA10 Program through the acceptance for filing of the first IND application with respect to the LCA10 Program.

We are entitled to receive clinical, regulatory, and launch milestone payments from Allergan up to a low-nine-digit amount in the aggregate and further commercial milestone payments up to a high-eight-digit amount in the aggregate with respect to each Collaboration Development Program for which Allergan exercises its Option, with certain of such milestone payments subject to reduction under certain circumstances. In the aggregate, we are eligible to receive clinical, regulatory, launch, and commercial milestone payments that could exceed $200.0 million for an indication in the first field per Collaboration Development Program, as well as the potential for additional regulatory milestones for indications in up to two additional fields. We are also entitled to receive royalties in the high-single digit percentages with respect to net sales of Licensed Products, subject to certain reductions under specified circumstances, and we will remain obligated to pay all license fees, milestone payments, and royalties due to its upstream licensors based on Allergan's exercise of its license rights with respect to Licensed Products. Allergan's obligation to pay royalties will expire on a country-by-country/Licensed Product-by-Licensed Product basis upon the latest of the expiration of patent-based exclusivity with respect to the applicable Licensed Product in the applicable country, expiration of regulatory-based exclusivity with respect to the applicable Licensed Product in the applicable country and the tenth anniversary of the first commercial sale by Allergan of the applicable Licensed Product in the applicable country. We are generally required to pay to Allergan royalties in the low- to mid-single digit percentages on net sales of products developed under Collaboration Development Programs that Allergan terminated following exercise of its Option, in each case over royalty terms equivalent to those for the royalties due to us under the agreement.

With respect to the LCA10 Program and up to one other Collaboration Development Program of our choosing, following the exercise by Allergan of its Option to such programs, we will have the right to elect to participate in a profit-sharing arrangement with Allergan in the United States, on terms mutually agreed by us and Allergan and subject to a right of Allergan to reject such election under certain circumstances, under which we and Allergan would share equally in net profits and losses on specific terms to be agreed between us and Allergan, in lieu of Allergan paying royalties on net sales of any applicable Licensed Products in the United States and in such event Allergan's milestone payment obligations would be reduced, with our being eligible to receive clinical, regulatory, and launch milestone

payments up to a low nine-digit amount in the aggregate and further commercial milestone payments up to a high-eight digit amount in the aggregate, subject to reduction under certain circumstances. If we elect to participate in a profit-sharing arrangement, we are obligated to reimburse Allergan for half of the development costs incurred by Allergan with respect to the applicable Collaboration Development Program and Allergan will retain control of all development and commercialization activities for the applicable Licensed Products. Under the agreement, we and Allergan will establish an alliance steering committee ("ASC") comprised of three members from each of us and Allergan, which will have review, oversight and decision-making responsibility for selecting the targets and indications and certain Option Package criteria for the Collaboration Development Programs and determining whether the Option Package criteria for a Collaboration Development Program have been satisfied. With respect to a given Collaboration Development Program, all decisions of the ASC will be made by consensus, subject to specified final decision-making rights, with each of us and Allergan having one vote.

During the Research Term, neither we nor any of our affiliates will, subject to specified exceptions in the agreement, develop, manufacture or commercialize any gene editing therapy in the ocular field, or grant a license or sublicense to develop, manufacture or commercialize any gene editing therapy in the ocular field. During the Research Term, neither Allergan nor any of its affiliates will, subject to specified exceptions in the agreement, develop, manufacture or commercialize, or grant a license or sublicense to develop, manufacture or commercialize, any gene editing therapy in the ocular field directed to any ocular indication to which any gene editing therapy in any non-terminated Collaboration Development Program is directed or the same target to which any gene editing therapy in any non-terminated Collaboration Development Program is directed. After the Research Term, neither we, Allergan nor any of their respective affiliates will, subject to specified exceptions in the agreement, develop, manufacture or commercialize, or grant a license or sublicense to develop, manufacture or commercialize, any gene editing therapy in the ocular field directed to any ocular indication to which any Licensed Product is directed or any target to which any Licensed Product is directed.

Unless earlier terminated, the term of the agreement will expire upon (i) the expiration of the Research Term if Allergan does not exercise any Option or (ii) the expiration of all payment obligations under the agreement. In addition to other termination rights, Allergan has the right to terminate the agreement (i) in its entirety for an uncured material breach by us and (ii) in its entirety for any reason on a program-by-program basis for the Collaboration Development Programs for which Allergan has exercised its Option with 90 days' written notice. Additionally, Allergan may terminate the Research Term (a) on a Collaboration Development Program-by-Collaboration Development Program basis upon written notice to us in the event of a change of control of us or (b) for all Collaboration Development Programs, provided that, Allergan will not have any right to exercise any Option for any such Collaboration Development Program following any such termination. If Allergan terminates the Agreement for our material breach, subject to Allergan's continued payment, reporting, and audit obligations under the agreement, Allergan has the right to retain all licenses granted under the agreement and Allergan will no longer have any diligence obligations with respect to the Licensed Products.

Intellectual Property Licenses

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 The Broad Institute, Inc. ("Broad") and the President and Fellows of Harvard College ("Harvard"), for specified patent rights. In December 2016, we amended and restated this license agreement and further amended the agreement in March 2017 (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 (the "Harvard Cas9-I Patent Rights"), certain patents co-owned by the Massachusetts Institute of Technology ("MIT") and Broad, certain patents co-owned by MIT, The Rockefeller University ("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. The March 2017 amendment to the Cas9-I License Agreement included 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, 2017, we have certain rights under 37 U.S. patents, 64 pending U.S. patent applications, 11 European patents and related validations, 38 pending European patent 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 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 (the "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 ("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 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 Cpf1 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 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. An interference was filed with respect to 12 U.S. patents and one U.S. patent application that are co-owned by Broad and MIT, and in some cases, Harvard, in-licensed by us under the Cas9-I License Agreement. For more information regarding this interference proceeding, see *Intellectual Property* below, "Risk Factors—Risks Related to Our Intellectual Property" in Part I, Item 1A, and "Legal Proceedings" in Part I, Item 3. We are responsible for the cost of the interference proceeding and appeal 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.

The Broad Institute—Cpf1 License Agreement

In December 2016, we entered into a license agreement with Broad, for specified patent rights ("Cpf1 Patent Rights") related primarily to Cpf1 compositions of matter and their use for gene editing (the "Cpf1 License Agreement"). Pursuant to the Cpf1 License Agreement, Broad, on behalf of itself, Harvard, MIT, Wageningen University ("Wageningen"), and the University of Tokyo ("Tokyo" and collectively with the other institutions, the "Cpf1 Institutions") granted us an exclusive, worldwide, royalty-bearing, sublicensable license to the Cpf1 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 (collectively, the "Exclusive Cpf1 Field"), as well as a non-exclusive, worldwide, royalty-bearing, sublicensable license to the Cpf1 Patent Rights for all other purposes, subject to certain limitations and retained rights. The licenses granted to us under the Cpf1 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 the National Institute of Health ("NIH") are joint owners on certain Cpf1 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 Cpf1 License Agreement, and as of December 31, 2017, we have certain rights under one U.S. patent, three pending U.S. patent applications, one European patent and related validations, two pending European patent applications, five pending PCT patent 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 Cpf1 Field. We are also required to achieve certain development milestones within specified time periods for products covered by the Cpf1 Patent Rights, with Broad having the right to terminate the Cpf1 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 Cpf1 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 Cpf1 Institutions according to the same terms as are provided in the Cpf1 License

Agreement and a statement that the Cpf1 Institutions are intended third party beneficiaries of the sublicense agreement for certain purposes.

The licenses granted to us under the Cpf1 License Agreement are subject to retained rights of the U.S. government in the Cpf1 Patent Rights and rights retained by the Cpf1 Institutions on behalf of themselves and other academic, government and non-profit entities, to practice the Cpf1 Patent Rights for research, teaching, or educational purposes. Our exclusive license rights also are subject to rights retained by the Cpf1 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 Cpf1 Patent Rights and licensed products as research products or research tools, or for research purposes.

Under the Cpf1 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 Cpf1 Patent Rights for the development and commercialization of a product that would be subject to our exclusive license grant from Broad (a "Cpf1 Third Party Proposed Product Request"), Broad may notify us of such request. A Cpf1 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 Cpf1 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 Cpf1 Third Party Proposed Product Request ("Cpf1 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 Cpf1 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 Cpf1 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 Cpf1 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 Cpf1 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 Cpf1 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 Cpf1 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 Cpf1 License Agreement to develop and commercialize products directed to such gene target.

Under the Cpf1 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 (the "Initial Promissory Notes") in an aggregate principal amount of $10.0 million. The Initial Promissory Notes bore interest at 4.8% per annum. Principal and interest on the Initial Promissory Notes were payable on the first anniversary of the issuance date (or if earlier, a specified period of time following a sale of our company). We could 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 was 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 were required to pay all remaining principal and accrued interest on the Initial Promissory Notes in cash within a specified

period following such event. We settled the Initial Promissory Notes in shares of our common stock in 2017 and they are no longer outstanding.

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 Cpf1 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 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 Cpf1 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 Cpf1 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 Cpf1 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 Cpf1 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 (“Market Cap Success Payments”) or sale of our company for consideration in excess of those thresholds, (“Company Sale Success Payments,” which with the Market Cap Success Payments, 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 Cpf1 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 March 2017, a Market Cap Success Payment in the amount of $5.0 million under the Cpf1 License Agreement became due upon our market capitalization reaching $750 million, and we issued promissory notes to Broad and Wageningen in the aggregate original principal amount of $5.0 million (the “March Success Payment Notes”). The principal and interest on the March Success Payment Notes was due and payable in August 2017. In August 2017, we issued an aggregate of 271,347 shares of our common stock to Broad and paid $0.4 million to Wageningen as payment of all outstanding principal and interest under the March Success Payment Notes. Upon such issuance and payment, the March Success Payment Notes were cancelled. In September 2017, Wageningen designated Broad as the recipient of any future promissory notes that are owed to Wageningen pursuant to the Cpf1 License Agreement.

In December 2017, a success payment in the amount of $5.0 million under the Cpf1 License Agreement became due upon our market capitalization reaching $1.0 billion for a specified period of time, and we issued a promissory note to Broad in the original principal amount of $5.0 million (the "December Cpf1 Success Payment Note"). The principal and interest on the December Cpf1 Success Payment Note was due and payable in May 2018. In January 2018, we issued 150,606 shares of our common stock to Broad as payment of all outstanding principal and interest under the December Cpf1 Success Payment Note. Upon such issuance and payment, the December Cpf1 Success Payment Note was cancelled.

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 Cpf1 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 Cpf1 Patent Rights. We have the right to provide input in the prosecution of the Cpf1 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 Cpf1 Patent Rights prior to the date of the Cpf1 License Agreement, and to reimburse Broad for expenses associated with the prosecution and maintenance of the Cpf1 Patent Rights following the date of the Cpf1 License Agreement.

We have the first right, but not the obligation, to enforce the Cpf1 Patent Rights with respect to our licensed products in the Exclusive Cpf1 Field so long as certain conditions are met, such as providing Broad and the applicable Cpf1 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 Cpf1 License Agreement will expire on a country-by-country basis, upon the expiration of the last to expire valid claim of the Cpf1 Patent Rights in such country. However, our royalty obligations, discussed above, may survive expiration or termination. We have the right to terminate the Cpf1 License Agreement at will upon four months' written notice to Broad. Either party may terminate the Cpf1 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 Cpf1 License Agreement immediately if we challenge the enforceability, validity, or scope of any Cpf1 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 with Broad for specified patent rights (the "Cas9-II Patent Rights") related primarily to certain Cas9 compositions of matter and their use for gene editing (the "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 ("Iowa," and collectively with the other institutions, 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 Cpf1 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 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, 2017, we have certain rights under 13 pending U.S. patent applications, 13 pending European patent applications, and other related patent applications in jurisdictions outside of the United States and Europe.

In December 2017, a success payment in the amount of $2.5 million under our Cas9-II License Agreement became due upon our market capitalization reaching $1.0 billion for a specified period of time, and we issued a promissory note to Broad in the original principal amount of $2.5 million (the "December Cas9-II Success Payment Note"). The principal and interest on the December Cas9-II Success Payment Note was due and payable in May 2018. In January 2018, we issued 75,303 shares of our common stock to Broad as payment of all outstanding principal and interest under the December Cas9-II Success Payment Note. Upon such issuance and payment, the December Cas9-II Success Payment Note was cancelled.

The General Hospital Corporation License Agreements

In August 2014, we entered into a license agreement with The General Hospital Corporation, d/b/a Massachusetts General Hospital ("MGH"), for specified patent rights (the "First License MGH Patent Rights") and specified know-how and biological materials (the "First MGH License Agreement"). 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, 2017, we have certain rights under two U.S. patents, 14 pending U.S. patent applications, one European patent and related validations, ten 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 (such field, 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.

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 with MGH for specified patent rights (the "Second License MGH Patent Rights" and such agreement, the "Second MGH License Agreement"). Pursuant to the Second MGH License Agreement, and as of December 31, 2017, we have certain rights under two issued U.S. patents, six pending U.S. patent applications, one pending European patent application, one pending PCT patent application, and other related patent applications in jurisdictions outside of the United States and Europe. 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 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 $1.0 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 (the "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 (the "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. In December 2017, an MGH Market Cap Success Payment of $2.0 million became due under our Second MGH License Agreement in connection with our market capitalization reaching $1.0 billion, which we settled in January 2018 through the issuance of 80,000 shares of our common stock to MGH.

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 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.

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 *S. aureus* Cas9, high-fidelity Cas9 nucleases and Cas9 PAM variants, self-inactivating forms of Cas9, Cas9 nickases, 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, 2017, we owned one U.S patent, 19 pending U.S. non-provisional patent applications, 16 pending European patent applications, 16 pending U.S. provisional patent applications, 16 pending Patent Cooperation Treaty (“PCT”) patent 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 U.S. patents and its U.S. and foreign counterpart applications are 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, three of these pending PCT patent applications and 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.

As of December 31, 2017, we in-licensed 44 U.S. patents, which include claims to compositions of matter, methods of use, and certain processes as well as approximately 103 pending U.S. non-provisional patent applications, 13 European patents and related validations, 66 pending European patent applications, six pending PCT patent 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 various universities and institutions 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 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 —Intellectual Property Licenses."

On January 11, 2016, the Patent Trial and Appeal Board of the USPTO (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. 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, in certain cases, Harvard. The declaration of interference defined the invention that was 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.

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.

Having filed a notice of appeal on April 12, 2017, the University of California, the University of Vienna, and Emmanuelle Charpentier filed an appeal brief to the Court of Appeals for the Federal Circuit on July 25, 2017 for review of the no interference-in-fact decision made by the PTAB in the interference proceeding. Broad filed its responsive brief on October 25, 2017. The University of California, the University of Vienna and Emmanuelle Charpentier filed a reply brief on November 22, 2017. It is uncertain when or in what manner the Federal Circuit will act on this 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.

Separately, ToolGen Inc. ("Toolgen") filed Suggestions of Interference in the USPTO on April 13, 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) 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 in the future become a party to similar proceedings or priority disputes in Europe or other foreign jurisdictions. On January 17, 2018, the European Patent Office Opposition Division (the "Opposition Division") revoked in the European Patent Office (the "EPO") a European patent that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard (European Patent No. EP 2,771,468 B1). On January 18, 2018, Broad, acting on behalf of itself, MIT and Harvard filed a notice of appeal to the Boards of Appeal of the EPO for review of the Opposition Division's decision to revoke this patent. It is uncertain when or in what manner the Boards of Appeal will act on this appeal. The Opposition Division has also initiated opposition proceedings against six other European patents that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard (European Patent Nos. EP 2,784,162 B1, EP 2,896,697 B1, EP 2,898,075 B1, EP 2,921,557 B1, EP 2,931,898 B1, and EP 3,009,511 B1), 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), and two European patents that we have in-licensed from Broad, acting on behalf of itself, MIT, Harvard and Rockefeller (European Patent Nos. EP 2,825,654 B1 and EP 2,840,140 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 2,825,654 B1, EP 2,840,140 B1, EP 2,896,697 B1, EP 2,898,075 B1, EP 2,921,557 B1, EP 2,931,898 B1, and/or EP 3,009,511 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 notices of opposition have been filed against one other European patent that we in-license from Broad, acting on behalf of itself, MIT and Harvard (European Patent No. EP 2,931,897 B1). The deadline for filing oppositions against this European patent is August 1, 2018. 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, 2017, we owned one U.S. patent, 19 pending U.S. non-provisional patent applications, 16 pending European patent applications, 16 pending U.S. provisional patent applications, 16 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 U.S. patents and its U.S. and 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, three of these pending PCT patent applications and 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 2038, excluding any additional term for patent term adjustments or patent term extensions.

As of December 31, 2017, we in-licensed 35 U.S. patents, 11 European patents and related validations, and over 500 pending patent applications, including approximately 91 pending U.S. non-provisional patent applications, 57 pending European patent applications, six 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 various universities and institutions. 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, 2017, we owned two pending U.S. non-provisional patent applications, one pending European patent application, one pending Canadian patent application, and one pending PCT patent application which are directed to compositions of matter, including guide RNAs directed to CEP290, and methods of use for the treatment of LCA10. If issued as a U.S. patent, and if the appropriate maintenance fees are paid, the U.S. patent applications 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, 2017, our registered trademark portfolio consisted of registrations in the United States for EDITAS, EDITAS in Stylized Letters and the Infinity Logo, registrations in Australia, China, the European Union, Japan and Switzerland for EDITAS, registrations in Australia, the European Union and Switzerland for the Infinity Logo and a registration in the European Union for UDITAS.

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, biotechnology companies, governmental agencies, and public and private research institutions. Any product candidates that we successfully develop and commercialize may compete with existing therapies and new therapies 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, Casebia Therapeutics, CRISPR Therapeutics, ERS Genomics, Exonics Therapeutics, 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 other genome editing technologies, including TALENs, meganucleases, Mega-TALs, and zinc finger nucleases. The companies developing these other 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, Audentes Therapeutics, Homology Medicines, Nightstar 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.

In addition, many of our current or potential competitors, either alone or with their collaboration partners, may have 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 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.

Manufacturing

We currently contract with third parties for the manufacturing of our materials for preclinical studies and 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. We expect third-party manufacturers to be capable of providing sufficient quantities of our program materials to meet anticipated needs for preclinical studies and clinical trials. 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 preclinical, 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 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 (the "PHSA") and the Federal Food, Drug and Cosmetic Act (the "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 FDA's 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 ("DOJ") and other governmental entities, including state agencies.

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 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 ("IRB") representing each clinical site before each clinical trial may be initiated;
- 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 ("GCP");
- preparation and submission to the FDA of a Biologic License Application ("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 ("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 ("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 Prescription Drug User Free Act ("PDUFA") 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 ("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.

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. 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 ("RAC") of the 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.

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. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical trial is not conducted under an IND, the sponsor must ensure that the trial complies with certain regulatory requirements of the FDA in order to use the trial as support for an IND or application for marketing approval. Specifically, the FDA requires that such trials be conducted in accordance with GCP, including review and approval by an independent ethics committee and informed consent from subjects. The GCP requirements encompass both ethical and data integrity standards for clinical trials. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign trials are conducted in a manner comparable to that required for clinical trials in the United States.

Further, each clinical trial must be reviewed and approved by an 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 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 ("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 ("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 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.

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 ("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. Under federal law, the submission of most BLAs is subject to an application user fee, which for federal fiscal year 2018 is $2,421,495 for an application requiring clinical data. The sponsor of an approved BLA is also subject to an annual program fee, which for fiscal year 2018 is $304,162. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

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 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 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 ("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, Priority Review and Regenerative Advanced Therapy 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, priority review designation and regenerative advanced therapy 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 ("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 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.

With passage of the 21st Century Cures Act (the "Cures Act") in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

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 ("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 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.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the DOJ, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

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 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 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.

For products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, FDA will meet early in the development process to discuss pediatric study plans with sponsors and FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than 90 days after FDA's receipt of the study plan.

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 ("BPCIA"). The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. As of January 1, 2018, the FDA has approved nine biosimilar products 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.

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. In July 2016, the FDA issued a draft guidance intended to assist sponsors of the drug therapeutic and *in vitro* companion diagnostic device on issues related to co-development of the products.

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.

The FDA previously has required *in vitro* companion diagnostics intended to select the patients who will respond to the product candidate to obtain pre-market approval ("PMA") simultaneously with approval of the therapeutic product candidate. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee, which exceeds $250,000 for most PMAs; for federal fiscal year 2018, the standard fee for review of a PMA is $310,764 and the small business fee is $77,691.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the Quality System Regulation, which covers the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

The 21st Century Cures Act

On December 13, 2016, President Obama signed the Cures Act into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increased funding for the FDA to spend on innovation projects. The new law also amends the Public Health Service Act ("PHSA") to reauthorize and expand funding for the NIH. The Cures Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges the NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the PHSA, Title III of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the existing priority review voucher program for certain drugs intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for drug applications determined to be material national security threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires the FDA to evaluate the potential use of "real world evidence" to help support approval of new indications for approved drugs; provides a new "limited population" approval pathway for antibiotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes the FDA to designate a drug as a "regenerative advanced therapy," thereby making it eligible for certain expedited review and approval designations.

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 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 ("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 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 2019. 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.

PRIME Designation in the EU

In March 2016, the European Medicines Agency ("EMA") launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority Medicines ("PRIME") scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated EMA contact and rapporteur from the Committee for Human Medicinal Products ("CHMP") or Committee for Advanced Therapies are appointed early in the PRIME scheme facilitating increased understanding of the product at the EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

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 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 ("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.

Under the centralized procedure, the 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.

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.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union (commonly referred to as "Brexit"). Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to the EU Treaty. Since the regulatory framework for pharmaceutical products in the United Kingdom. covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

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 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) 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 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 ("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 ("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 ("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;
- 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" 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 ("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. The American Taxpayer Relief Act of 2012, which was enacted in January 2013, 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.

These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

Further, since enactment of the PPACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain PPACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Congress will likely consider other legislation to replace elements of the PPACA, during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the PPACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the PPACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction ("CSR") payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the PPACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

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.

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.

Foreign Operations

We did not have any foreign operations in any of the fiscal years ended December 31, 2017, 2016 and 2015.

Employees

As of January 1, 2018, we had 112 full-time employees, including 41 employees with M.D. or Ph.D. degrees. Of these full-time employees, 75 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.

Segment Reporting and Financial and Geographical Information

We are engaged solely in the discovery and development of medicines in the field of genome editing. Accordingly, we have determined that we operate in one operating segment. For segment and geographical financial information, see Note 2, *Summary of Significant Accounting Policies*, to the financial statements appearing elsewhere in this Annual Report on Form 10-K, which are incorporated herein by reference. Financial information about our research and development expenses in each of the last three fiscal years is provided in Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations" and is incorporated herein by reference.

Our Corporate Information

We were incorporated under the name Gengine, Inc. as a Delaware corporation 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 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., 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.

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 $120.3 million, $97.2 million, and $72.9 million for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017, we had an accumulated deficit of $305.9 million. We have financed our operations primarily through public offerings of our common stock, private placements of our preferred stock, our collaboration with Juno Therapeutics, Inc. ("Juno Therapeutics"), and an upfront payment from Allergan Pharmaceuticals International Limited ("Allergan"). 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 ("cGMP") manufacturing facility; and
- continue to 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

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 and 2017 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, cash equivalents, and marketable securities at December 31, 2017, anticipated interest income, and anticipated research support under our collaboration agreement with Juno Therapeutics, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 24 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 or natural history study 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 and our strategic alliance with Allergan;
- 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);
- whether Allergan exercises any of its options under our strategic alliance;
- 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 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 significant committed external source of funds, other than our right to payments under our collaboration agreement with Juno Therapeutics, and payments from our subtenant, 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.

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 arrangements;
- 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 (the "FDA"), the European Medicines Agency (the "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 therapeutic 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 therapeutic 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 a limited number of gene therapy products that have received marketing authorization from the FDA and the European Commission. 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 Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research ("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 ("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 (the "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 ("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 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. Notwithstanding, we are aware of certain groups conducting research in human embryo genome editing.

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, our agreement with CFFT and our strategic alliance with Allergan, 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 ("TALE") nucleases, 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 TALE 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

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 type 10 ("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 ("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 (a "BLA") to the FDA or a marketing authorization application (an "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 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, combined with CRISPR technology, have a limited, if any, history of being tested clinically. 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 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 ("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 a limited, if any, history of being evaluated in human clinical trials. 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 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 therapeutic 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 (“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 (“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;
- 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;
- 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 genome 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;
- 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 program is focused on a rare genetically defined disease with a limited patient pool from which to draw for enrollment in a clinical trial, as 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.

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 Leber Congenital Amaurosis ("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 affected.

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.

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 authorities;
- 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 the 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
- 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.

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 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. 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. 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 or therapies using CRISPR technology include Caribou Biosciences, Casebia Therapeutics, 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, Audentes Therapeutics, Exonic Therapeutics, Homology Medicines, Nightstar 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, may 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.

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 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.

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 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.

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.

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, and, in March 2017, we entered into a strategic alliance with Allergan focused on discovering, developing, and commercializing new gene editing medicines for a range of ocular disorders. 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 and, in the case of our strategic alliance with Allergan, whether they exercise an option to commercialize a product. 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, and alliance arrangements we may enter into under which our research programs may be involved and potential product candidates may be developed, including our strategic alliance with Allergan, pose the following risks to us:

- Collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations.
- 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.
- 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.
- 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.
- 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, as the case may be. 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 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 or allies. 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.

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 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 (the "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 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. ("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.

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 Broad and the President and Fellows of Harvard College ("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 "Part I—Business—Our Collaborations and Licensing Strategy" in this Annual Report on Form 10-K. 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, and The General Hospital Corporation, d/b/a Massachusetts General Hospital, 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 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. In connection with these reimbursement obligations, we incurred expenses in aggregate of $18.7 million, $23.6 million, and $9.4 million during the years ended December 31, 2017, 2016, and 2015, respectively.

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 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 priority and validity disputes. In addition, our owned and in-licensed patents and other intellectual property may be subject to further priority and validity disputes, and other similar intellectual property proceedings including inventorship disputes. 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 ("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 the Massachusetts Institute of Technology ("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 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.

Having filed a notice of appeal on April 12, 2017, the University of California, the University of Vienna, and Emmanuelle Charpentier filed an appeal brief to the Court of Appeals for the Federal Circuit on July 25, 2017 for review of the no interference-in-fact holding made by the PTAB in the interference proceeding. Broad filed its responsive brief on October 25, 2017. The University of California, the University of Vienna and Emmanuelle Charpentier filed a reply brief on November 22, 2017. It is uncertain when or in what manner the Federal Circuit will act on this 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. ("ToolGen") filed Suggestions of Interference in the USPTO on April 13, 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) 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.

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. On January 17, 2018, the European Patent Office Opposition Division (the "Opposition Division") revoked in the European Patent Office ("EPO") a European patent that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard (European Patent No. EP 2,771,468 B1). On January 18, 2018, Broad, acting on behalf of itself, MIT and Harvard filed a notice of appeal to the Boards of Appeal of the EPO for review of the Opposition Division's decision to revoke this patent. It is uncertain when or in what manner the Boards of Appeal will act on this appeal. The Opposition Division has also initiated opposition proceedings against six other European patents that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard (European Patent Nos. EP 2,784,162 B1, EP 2,896,697 B1, EP 2,898,075 B1, EP 2,921,557 B1,EP 2,931,898 B1, and EP 3,009,511 B1), 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), and two European patents that we have in-licensed from Broad, acting on behalf of itself, MIT, Harvard and The Rockefeller University ("Rockefeller") (European Patent Nos. EP 2,825,654 B1 and EP 2,840,140 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 2,825,654 B1, EP 2,840,140 B1, EP 2,896,697 B1, EP 2,898,075 B1, EP 2,921,557 B1, EP 2,931,898 B1, and/or EP 3,009,511 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 notices of opposition have been filed against one other European patent that we in-license from Broad, acting on behalf of itself, MIT and Harvard (European Patent No. EP 2,931,897 B1). The deadline for filing oppositions against this European patent is August 1, 2018. 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 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. Both of these petitions were denied by the respective District Court and, in one of these two actions, Intellia Therapeutics has filed a notice of appeal to the United States Court of Appeals. 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, re-examinations, 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 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 ("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 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, including the amount, if any, that may become due and payable to our licensors in connection with sublicense income. If these events were to occur, they 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.

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 third party patents and patent applications that may be construed to cover our CRISPR technology and product candidates. In order to avoid infringing these third party patents, or patents that issue from these third party patent applications, 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 in 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 our CRISPR technology and product candidates we may develop. 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 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 (the "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. 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.

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 were to initiate 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 nine 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. The opposition proceedings have so far resulted in the revocation of one of our in-licensed European patents. In view of certain arguments made by the third parties against this revoked patent and similar arguments made by the third parties against additional other in-licensed European patents under opposition, the opposition proceedings could potentially lead to the revocation of additional in-licensed European patents. These and other proceedings could result in the revocation or 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 patents and patent applications in this landscape that may 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 2013/141680 (and its related U.S. Patent No. 9,637,739 and other related U.S. patent applications and foreign counterparts) filed by Vilnius University (which is reported to have exclusively licensed its rights to DuPont Pioneer, which is reported to have licensed certain rights to Caribou Biosciences, which is reported to have non-exclusively licensed certain rights to Intellia Therapeutics and CRISPR Therapeutics), WO 2013/176772 (and its related U.S. patent applications and foreign counterparts including European Patent No. EP 2,800,811 B1, which is being opposed by several parties) filed by the 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), WO 2014/065596 (and its related U.S. patent applications and foreign counterparts) filed by ToolGen, and WO 2014/089290 (and its related U.S. patent applications and foreign counterparts including European Patent No. EP 3,138,910 B1, which is being opposed by several parties) filed by Sigma-Aldrich Co. LLC. We are also aware of U.S. Patent No. 9,738,908 filed by System Biosciences, LLC which is currently under re-examination. 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.

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 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 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 (the "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;
- 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 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.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

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;
- 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;

- the federal Health Insurance Portability and Accountability Act of 1996, as further amended by the Health Information Technology for Economic and Clinical Health Act, 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, which 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, which 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 certain state laws that 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 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.

The efforts of the Administration to pursue regulatory reform may limit the FDA's ability to engage in oversight and implementation activities in the normal course, and that could negatively impact our business.

The Trump Administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. On January 30, 2017, President Trump issued an executive order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Recently enacted and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, 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 any future collaborators, may receive for any approved products.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (the "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, as amended by the Health Care and Education Affordability Reconciliation Act (the "PPACA"), which became law in 2010, contains provisions of importance to our business, including, without limitation, our ability to commercialize and the prices we may obtain for any of our product candidates and that are approved for sale, the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of federal healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- 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 drug samples that manufacturers and distributors provide to physicians; and
- 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. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to 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. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our potential products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

With the new Trump Administration and Congress, there may be additional legislative changes, including potentially repeal and replacement of certain provisions of the PPACA. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate" of the PPACA. The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the PPACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the PPACA. The Congress will likely consider other legislation to replace elements of the PPACA, during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the PPACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the PPACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction ("CSR") payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the PPACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

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.

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.

On August 3, 2017, the Congress passed the FDA Reauthorization Act of 2017 ("FDARA"). FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

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.

The Foreign Corrupt Practices Act ("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 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, Managing Growth and Information Technology

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.

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, clinical development, manufacturing, and sales and marketing. For example, our total number of employees grew from 55 as of December 31, 2015 to 112 as of January 1, 2017. 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.

Security breaches and other disruptions to our information technology structure could compromise our information, disrupt our business and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we collect, process and store sensitive data, including intellectual property, as well as our proprietary business information and that of our suppliers and business partners, employee data, and we expect to collect personally identifiable information of clinical trial participants when we begin clinical trials. We also rely to a large extent on information technology systems to operate our business. We have outsourced elements of our confidential information processing and information technology structure, and as a result, we are managing independent vendor relationships with third parties who may or could have access to our confidential information. Similarly, our business partners and other third-party providers possess certain of our sensitive data. The secure maintenance of this information is important to our operations and business strategy. Despite our security measures, our information technology infrastructure (and those of our partners, vendors and third-party providers) may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. We, our partners, vendors, and other third-party providers could be susceptible to third party attacks on our, and their, information security systems, which attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including organized criminal groups, hacktivists, nation states and others. While we have invested in information technology security measures and the protection of confidential information, there can be no assurance that our efforts will prevent service interruptions or security breaches. Any such interruptions or breach may substantially impair our ability to operate our business and would compromise our, and their, networks and the information stored could be accessed, publicly disclosed, lost, or stolen. Any such access, disclosure, or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disrupt our operations, and damage our reputation, any of which could adversely affect our business.

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 and clinical 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;
- 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;
- 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 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 significant 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.

We 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 volume limitations applicable to affiliates. In addition, under the terms of certain of our license agreements and certain 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 subject to rights requiring us to register such shares under the Securities Act of 1933, as amended (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.

Certain of our executive officers, directors, and 5% stockholders, if they choose to act together, maintain the ability to significantly influence all matters submitted to stockholders for approval.

As of December 31, 2017, certain of our executive officers, directors, and a small group of 5% stockholders in the aggregate beneficially owned shares representing a meaningful percentage of our outstanding common stock. As a result, these stockholders, if they act together, may 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 (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 ("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 our proxy statement for our 2018 Annual Meeting of Stockholders, we will not include all of the executive compensation related information that would be required if we were not an emerging growth company. 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.

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 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 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 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 "Item 1A. 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 ("PTAB") of the United States Patent and Trademark Office ("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 The Broad Institute, Inc. ("Broad"), the Massachusetts Institute of Technology ("MIT"), and in some cases the President and Fellows of Harvard College ("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.

Having filed a notice of appeal on April 12, 2017, the University of California, the University of Vienna, and Emmanuelle Charpentier filed an appeal brief to the Court of Appeals for the Federal Circuit on July 25, 2017 for review of the no interference-in-fact holding made by the PTAB in the interference proceeding. Broad filed its responsive brief on October 25, 2017. The University of California, the University of Vienna and Emmanuelle Charpentier filed a reply brief on November 22, 2017. It is uncertain when or in what manner the Federal Circuit will act on this appeal.

Separately, ToolGen Inc. ("ToolGen") also filed Suggestions of Interference in the USPTO on April 13, 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.

On January 17, 2018, the European Patent Office Opposition Division (the "Opposition Division") revoked in the European Patent Office ("EPO") a European patent that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard (European Patent No. EP 2,771,468 B1). On January 18, 2018, Broad, acting on behalf of itself, MIT and Harvard filed a notice of appeal to the Boards of Appeal of the EPO for review of the Opposition Division's decision to revoke this patent. It is uncertain when or in what manner the Boards of Appeal will act on this appeal. The Opposition Division has also initiated opposition proceedings in the EPO against six other European patents that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard, one European patent that we have in-licensed from Broad, acting on behalf of itself and MIT and two European patents that we have in-licensed from Broad, acting on behalf of itself, MIT, Harvard and The Rockefeller University. In addition, notices of opposition have been filed against one other European patent that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard.

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 (the "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 each quarter in the years ended December 31, 2016 and 2017:

	Market Price	
2017	**High**	**Low**
First Quarter	$ 29.20	$ 16.30
Second Quarter	$ 22.74	$ 13.12
Third Quarter	$ 24.50	$ 15.28
Fourth Quarter	$ 32.85	$ 20.29

	Market Price	
2016	**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, 2018, we had approximately 26 holders of record of our common stock. This number does not include beneficial owners whose shares were held in street name.

Dividend Policy

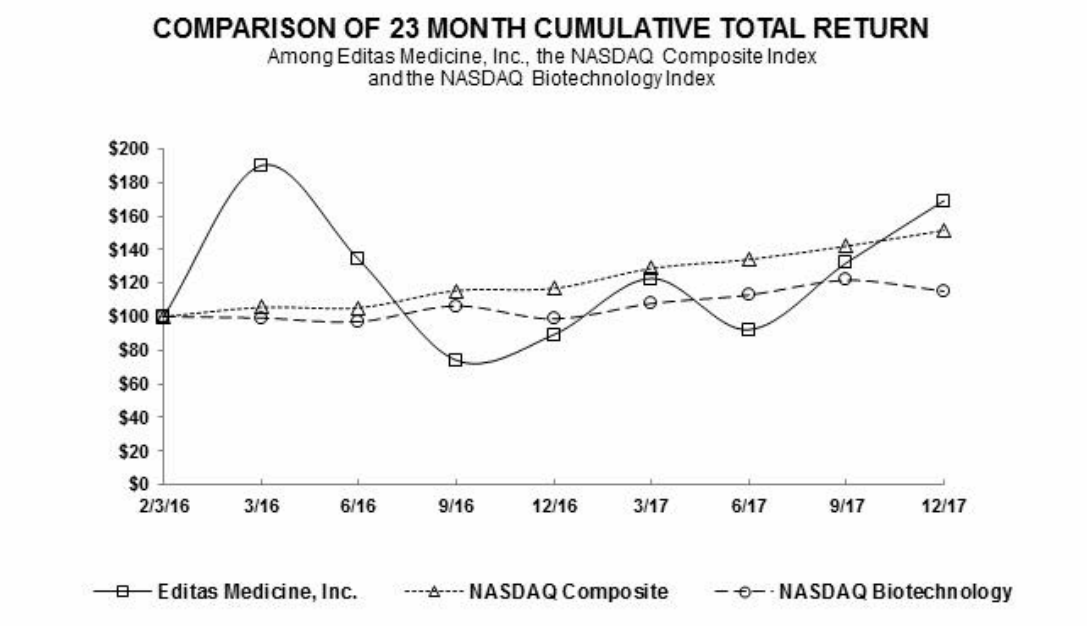
We have never declared or paid any cash dividends on our common stock. We currently intend to retain future earnings to fund the development and growth of our business. We do not expect to pay any cash dividends in the foreseeable future. In addition, the terms of any future debt agreements that we may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

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 (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 (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, 2017. The comparison assumes $100 was invested after the market closed on

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.



Recent Sales of Unregistered Securities

In December 2017, in connection with the triggering of a success payment under our Cpf1 License Agreement and our Cas9-II License Agreement, we issued promissory notes (the "Notes"), in an aggregate principal amount of $7.5 million to the Broad Institute, Inc. The Notes were 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.

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 (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, 2017, we had used all of the net offering proceeds, primarily to fund preclinical studies for our lead program, continued expansion of our platform technology, and preclinical studies of our research programs, as well as for working capital and general corporate purposes. There was no material change in our use of the net proceeds from the offering from that described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act.

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, 2017, 2016 and 2015 and the consolidated balance sheet data as of December 31, 2017 and 2016 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, 2014 and 2013 and consolidated balance sheet data as of December 31, 2015, 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.

	Year Ended December 31,				Period from September 3, 2013 (Inception) to December 31,
	2017	2016	2015	2014	2013
	(in thousands, except share and per share data)				
Consolidated Statements of Operations Data:					
Collaboration and other research and development revenues	$ 13,728	$ 6,053	$ 1,629	$ —	$ —
Operating expenses:					
Research and development	83,159	56,979	18,846	5,073	530
General and administrative	50,502	46,262	18,095	7,650	1,210
Total operating expenses	133,661	103,241	36,941	12,723	1,740
Operating loss	(119,933)	(97,188)	(35,312)	(12,723)	(1,740)
Other income (expense), net	587	(57)	(37,445)	(928)	(18)
Interest income (expense), net	(978)	62	(143)	(34)	—
Total other income (expense), net	(391)	5	(37,588)	(962)	(18)
Net loss	$ (120,324)	$ (97,183)	$ (72,900)	$ (13,685)	$ (1,758)
Reconciliation of net loss to net loss attributable to common stockholders:					
Net loss	$ (120,324)	$ (97,183)	$ (72,900)	$ (13,685)	$ (1,758)
Accretion of redeemable convertible preferred stock to redemption value	—	(47)	(394)	(309)	(25)
Net loss attributable to common stockholders [1]	$ (120,324)	$ (97,230)	$ (73,294)	$ (13,994)	$ (1,783)
Net loss per share attributable to common stockholders, basic and diluted [1]	$ (2.98)	$ (3.02)	$ (28.55)	$ (12.46)	$ (5.93)
Weighted-average common shares outstanding, basic and diluted [1]	40,323,631	32,219,717	2,566,916	1,123,098	300,480

(1) See Note 15 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.

	December 31,				
	2017	2016	2015	2014	2013
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents, and marketable securities	$ 329,139	$ 185,323	$ 143,180	$ 10,623	$ 2,012
Working capital	295,492	154,100	138,060	4,555	(39)
Total assets	373,260	229,182	149,363	12,188	2,481
Deferred revenue, net of current portion	94,725	26,000	25,321	—	—
Construction financing lease obligation, net of current portion	33,431	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)	208,080	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 I, 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 developing transformative genomic medicines with the aim to treat a broad range of serious diseases. The promise of genomic medicines is supported by the advancing knowledge of the human genome, and harnessing the progress in technologies for cell therapy, gene therapy, and, most recently, genome editing. We believe this progress sets the stage for us to create unprecedented medicines with the potential to have a durable benefit for patients. At Editas Medicine, our core capability in genome editing uses the technology known as CRISPR (clustered, regularly interspaced, short palindromic repeats) with which we can create molecules that efficiently and specifically edit DNA. Our mission is to translate the promise of this science into a broad class of medicines to help people living with serious diseases around the world. To this end, we have developed a proprietary genome editing platform based on CRISPR technology and we continue to expand its capabilities. Our initial product development strategy is to primarily target genetically defined diseases with a focus on debilitating illnesses where there are poor or no approved treatments and where the genetic basis of disease is well understood. 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. While our discovery efforts have ranged across several different diseases and therapeutic areas, the two areas where our programs are more mature are ocular diseases and engineered cell medicines. Our most advanced program is designed to address a specific genetic form of retinal degeneration called Leber Congenital Amaurosis type 10 ("LCA10"), a disease for which we are not aware of any available therapies and which we are aware of only one potential treatment in clinical trials in the United States and Europe. We aim to file an investigational new drug ("IND") application by mid-2018 for our LCA10 program. In May 2015, we entered into a collaboration with Juno Therapeutics, Inc. ("Juno Therapeutics"), a leader in the emerging field of immuno-oncology, to develop novel engineered T cell therapies for cancer and, in March 2017, we entered into a strategic alliance and option agreement with Allergan Pharmaceuticals International Limited ("Allergan"), a wholly-owned subsidiary of Allergan plc, a leading global pharmaceutical company, to discover, develop, and commercialize new gene editing medicines for a range of ocular disorders.

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 (the "IPO"), follow-on public offerings of our common stock including through an at-the-market offering, private placements of our preferred stock, payments received under our collaboration with Juno Therapeutics, and the upfront payment that we received under our strategic alliance with Allergan. From inception through December 31, 2017, we raised an aggregate of $545.5 million to fund our operations. We raised an additional $48.5 million in net proceeds from an at-the-market offerings of our common stock in January 2018.

In February 2016, we completed our IPO and received aggregate net proceeds of approximately $97.5 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. In March 2017, we completed a follow-on offering and received net proceeds of approximately $96.7 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. In December 2017, we completed another follow-on offering and received net proceeds of approximately $57.2 million, after deducting underwriting discounts and other offering expenses payable by us. During January 2018, we completed at-the-market offerings and received net proceeds of approximately $48.5 million.

Since inception, we have incurred significant operating losses. Our net losses were $120.3 million, $97.2 million and $72.9 million for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017, we had an accumulated deficit of $305.9 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, 2018 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 each of May 2016 and July 2017, 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, 2017, we had recognized an aggregate of $12.2 million of research support from Juno Therapeutics since entering into the agreement, including $5.0 million recognized in connection with the achievement of development milestones under the collaboration related to technical progress in two of the three research programs under the collaboration. In connection with entering into our strategic alliance with Allergan in March 2017, we received an upfront payment of $90.0 million from Allergan (such payment, the "Allergan Upfront"). For the year ended December 31, 2017, we recognized $8.8 million in revenue in connection with the Allergan Upfront. As of December 31, 2017, we recorded $81.2 million of deferred revenue, of which $68.3 million is classified as long-term on the consolidated balance sheet. For additional information about our revenue recognition policy related to the Juno Therapeutics collaboration or the Allergan agreement, see "—Critical Accounting Policies and Estimates—Revenue Recognition."

For the foreseeable future, we expect substantially all of our revenue will be generated from our collaboration with Juno Therapeutics, our strategic research alliance with Allergan to the extent Allergan exercises any of its options, any other collaborations or agreements we may enter into and anticipated interest income.

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, including any sublicensing or success payments made to our licensors.

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, IND-enabling studies and natural history 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 a product, if and when approved, whether alone or in collaboration with others;
- acceptance of a 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.

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.

We do not track research and development costs on a program-by-program basis.

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 and prepare for the clinical development 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, information technology, facilities, 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 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. ("Broad") and the President and Fellows of Harvard College ("Harvard") as described in more detail in Part I, Item 1A "Risk Factors—Risks Related to Our Intellectual Property," we anticipate general and administrative expenses will continue to be significant. Some of our in-licensed patents under our license agreement with Broad and Harvard are subject to priority disputes, and we anticipate that our obligation to reimburse Broad and Harvard for expenses related to these interference and opposition proceedings during future periods will be substantial until such proceedings are resolved.

Other Income (Expense), Net

Other income (expense), net consists primarily of interest expense on our construction financing lease obligation and promissory notes, and amortization of premiums associated with marketable securities, partially offset by rental income from our subtenant, interest income, and accretion of discounts associated with marketable securities.

Prior to 2017, other income (expense), net consisted 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 our liability for a warrant to purchase preferred stock. Upon the completion of the IPO, 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, there were no further remeasurement gains or losses associated with the warrant after the first quarter of 2016.

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 United States 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 assets and 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, 2017, revenue to date has primarily been generated from our collaboration agreement with Juno Therapeutics and our strategic alliance with Allergan. We recognize revenue in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("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 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* ("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).

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 ("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 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 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*, 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.

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.

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.

Stock-based Compensation

We account for our 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 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,		
	2017	2016	2015
Expected volatility	77.8 %	78.4 %	78.8 %
Expected term (in years)	6.25	6.25	6.25
Risk-free interest rate	2.1 %	1.5 %	1.7 %
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 during 2016 and 2015 were as follows. There were no stock options granted to non-employees during 2017:

	Year Ended December 31,		
	2017	2016	2015
Expected volatility	—	76.5 %	80.0 %
Expected term (in years)	—	10.0	10.0
Risk-free interest rate	—	1.6 %	2.2 %
Expected dividend yield	—	—	—

Stock-based compensation totaled approximately $23.4 million, $16.9 million, and $3.5 million for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017, we had $10.3 million and $33.4 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 4.7 and 2.5 years, respectively. We expect the impact of our stock-based compensation expense for restricted stock and stock 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.

Results of Operations

Comparison of Years ended December 31, 2017 and 2016

The following table summarizes our results of operations for the years ended December 31, 2017 and 2016, together with the changes in those items in dollars (in thousands) and the respective percentage of changes, unless greater than 100% or less than (100)%, in which case we denoted such changes as not meaningful (n/m):

	Year Ended December 31,			
	2017	2016	Dollar Change	Percentage Change
Collaboration and other research and development revenues	$ 13,728	$ 6,053	$ 7,675	n/m
Operating expenses:				
Research and development	83,159	56,979	26,180	46 %
General and administrative	50,502	46,262	4,240	9 %
Total operating expenses	133,661	103,241	30,420	29 %
Other income (expense), net				
Other income (expense), net	587	(57)	644	n/m
Interest (expense) income, net	(978)	62	(1,040)	n/m
Total other (expense) income, net	(391)	5	(396)	n/m
Net loss	$ (120,324)	$ (97,183)	$ (23,141)	(24) %

Collaboration and Other Research and Development Revenues

Collaboration and other research and development revenues were $13.7 million for the year ended December 31, 2017 and consisted of $8.8 million of revenue recognized pursuant to our strategic alliance with Allergan and $4.9 million of revenue recognized pursuant to our collaboration with Juno Therapeutics, of which $2.5 million related to a milestone payment.

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 Cystic Fibrosis Foundation Therapeutics, Inc. (“CFFT”).

Research and Development Expenses

Research and development expenses increased by $26.2 million, to $83.2 million for the year ended December 31, 2017 from $57.0 million for the year ended December 31, 2016. The following table summarizes our research and development expenses for the years ended December 31, 2017 and December 31, 2016, together with the changes in those items in dollars (in thousands) and the respective percentages of change:

	Year Ended December 31,			
	2017	2016	Dollar Change	Percentage Change
Process and platform development expenses	$ 17,117	$ 9,579	$ 7,538	79 %
Stock-based compensation expenses	15,131	12,647	2,484	20 %
Licensing and sublicensing payment expenses	14,610	18,469	(3,859)	(21) %
Success payment expenses	14,500	—	14,500	100 %
Employee related expenses	14,406	9,095	5,311	58 %
Facility expenses	4,416	5,671	(1,255)	(22) %
Other expenses	2,979	1,518	1,461	96 %
Total research and development expenses	$ 83,159	$ 56,979	$ 26,180	46 %

The increase in research and development expenses for the year ended December 31, 2017 compared to the year ended December 31, 2016 was primarily attributable to:

- approximately $14.5 million in increased success payments due to the triggering of multiple success payment obligations under licensing agreements with Broad and The General Hospital Corporation, d/b/a Massachusetts General Hospital ("MGH");
- approximately $7.5 million in increased process and platform development expenses due to increased research activity, mostly relating to external research and development spend which we expect will increase further as we continue to support the preclinical studies and prepare for clinical development for our LCA10 program as well as our other research programs;
- approximately $5.3 million in increased employee related expenses due to an increase in the size of our workforce;
- approximately $2.5 million in increased stock based compensation expense due to an increase in employee stock option expense and non-employee restricted stock expense; and
- approximately $1.5 million in increased other expenses due to increased professional service and office expenses.

These increases were partially offset by an approximate $3.8 million decrease in licensing and sublicensing payment expenses due pursuant to license agreements that were executed in 2016 with Broad and MGH, partially offset by a sublicensing fees in 2017 due to certain of our licensors in connection with receiving the Allergan Upfront, and an approximately $1.3 million decrease in facility related expenses.

General and Administrative Expenses

General and administrative expenses increased by $4.2 million, to $50.5 million for the year ended December 31, 2017 from $46.3 million for the year ended December 31, 2016. The following table summarizes our general and administrative expenses for the year ended December 31, 2017 and December 31, 2016, together with the changes in those items in dollars (in thousands) and the respective percentages of change:

	Year Ended December 31,			
	2017	2016	Dollar Change	Percentage Change
Intellectual property and patent related fees	$ 23,921	$ 26,963	$ (3,042)	(11) %
Professional service expenses	6,010	5,483	527	10 %
Employee related expenses	8,915	6,881	2,034	30 %
Stock-based compensation expenses	8,233	4,234	3,999	94 %
Other expenses	3,423	2,701	722	27 %
Total general and administrative expenses	$ 50,502	$ 46,262	$ 4,240	9 %

The increase in general and administrative expenses for the year ended December 31, 2017 compared to the year ended December 31, 2016 was primarily attributable to:

- approximately $4.0 million in increased stock-based compensation expenses due to an increase in employee stock option expense;
- approximately $2.0 million in increased employee related expenses due to an increase in the size of our workforce;
- approximately $0.7 million in increased other expenses including facility-related expenses; and
- approximately $0.5 million in increased professional services expenses.

These increases were partially offset by an approximate $3.0 million decrease in intellectual property and patent related fees, including expenses associated with the prosecution and maintenance of patents and patent applications, which was primarily due to the fact that our in-licensors had additional legal costs during the year ended December 31, 2016 due to the nationalization of certain patent applications and preparing for a U.S. patent interference proceeding.

Other Income (Expense), Net

For the year ended December 31, 2017, other income (expense), net was an expense of $0.4 million, which was primarily attributable to interest expense on our construction financing lease obligation and certain promissory notes, and amortization of premiums associated with marketable securities, partially offset by rental income from our subtenant, interest income, and accretion of discounts associated with marketable securities.

For the year ended December 31, 2016, other income (expense), net was income of $5 thousand, which was primarily attributable to interest income earned on our cash equivalents and government grant income, partially offset by interest expense on our construction financing lease obligation and loss on disposal of equipment.

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) and respective percentages of change:

	Year Ended December 31,			
	2016	2015	Dollar Change	Percentage Change
Collaboration and other research and development revenues	$ 6,053	$ 1,629	$ 4,424	n/m
Operating expenses:				
Research and development	56,979	18,846	38,133	n/m
General and administrative	46,262	18,095	28,167	n/m
Total operating expenses	103,241	36,941	66,300	n/m
Other income (expense), net:				
Other expense, net	(57)	(37,445)	37,388	n/m
Interest income (expense), net	62	(143)	205	n/m
Total other income (expense), net	5	(37,588)	37,593	n/m
Net loss	$ (97,183)	$ (72,900)	$ (24,283)	(33) %

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) and the respective percentages of change:

	Year Ended December 31,			
	2016	2015	Dollar Change	Percentage Change
Licensing and sublicensing payment expenses	$ 18,469	$ 4,603	$ 13,866	n/m
Stock-based compensation expenses	12,647	3,015	9,632	n/m
Process and platform development expenses	9,579	3,957	5,622	n/m
Employee related expenses	9,095	4,399	4,696	n/m
Facility expenses	5,671	1,805	3,866	n/m
Other expenses	1,518	1,067	451	42 %
Total research and development expenses	$ 56,979	$ 18,846	$ 38,133	n/m

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 $13.9 million in increased license fees related to our license agreements that were executed in 2016 with MGH and 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 $9.6 million in increased stock-based compensation expense due to an increase in employee stock option expense and non-employee restricted stock expense;
- approximately $5.6 million in increased process and platform development costs due to increased research activity;
- approximately $4.7 million in increased employee related expenses, resulting from an increase in the size of our workforce and the hiring of key executives throughout 2016;
- 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 $0.5 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 following table summarizes our general and administrative expenses for the years ended December 31, 2016 and December 31, 2015, together with the changes in those items in dollars (in thousands) and the respective percentages of change:

	Year Ended December 31,			
	2016	2015	Dollar Change	Percentage Change
Intellectual property and patent related fees	$ 26,963	$ 10,475	$ 16,488	n/m
Employee related expenses	6,881	3,146	3,735	n/m
Professional service expenses	5,483	3,144	2,339	74 %
Stock-based compensation expenses	4,234	498	3,736	n/m
Other expenses	2,701	832	1,869	n/m
Total general and administrative expenses	$ 46,262	$ 18,095	$ 28,167	n/m

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

- approximately $16.5 million in increased intellectual property legal and patent related fees, including expenses associated with patents and patent applications, including expenses associated with the prosecution and maintenance of such patents and patent applications, which was primarily due to the fact that our in-licensors had additional legal costs during the year ended December 31, 2016 due to the nationalization of certain patent applications and preparing for the U.S. patent interference proceeding;
- approximately $3.7 million in increased stock-based compensation expenses;
- approximately $3.7 million in increased employee compensation cost, resulting from an increase in the size of our workforce and the hiring of key executives in 2016;
- approximately $2.3 million in increased professional service expenses; and
- approximately $1.9 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

For the year ended December 31, 2016, other income (expense), net was income of $5 thousand, which was primarily attributable to interest income earned on our cash equivalents and government grant income, partially offset by interest expense on our construction financing lease obligation and loss on disposal of equipment.

For the year ended December 31, 2015, other income (expense), net was an expense of $37.6 million, which was primarily related to mark-to-market adjustments in our Series A preferred stock tranche right liability and mark-to-market adjustments for the anti-dilution protection liability related to our issuance of common stock to our licensors. The tranche right liability and anti-dilution liability were both settled in June 2015.

Liquidity and Capital Resources

Sources of Liquidity

From inception through December 31, 2017, we funded our operations primarily through proceeds from private placements of our preferred stock of $163.3 million, net proceeds of $251.4 million from public offerings of our common stock, the Allergan Upfront, and an up-front payment, research and development payments, and milestone payments under our collaboration with Juno Therapeutics of $25.0 million, $8.1 million and $5.0 million, respectively. As of December 31, 2017, we had cash, cash equivalents, and marketable securities of $329.1 million.

In addition to our existing cash, cash equivalents, and marketable securities, we are eligible to earn milestone payments and are entitled to cost reimbursement under our collaboration agreement with Juno Therapeutics. Additionally, under our strategic alliance with Allergan, we are eligible to earn milestone payments. Our ability to earn the milestone payments and the timing of earning these amounts are dependent upon the timing and outcome of our development, regulatory and commercial activities, as well as whether Allergan exercises any of its options under the strategic alliance, and, as such, are uncertain at this time. As of December 31, 2017, our right to payments under our collaboration agreement with Juno Therapeutics and our strategic alliance with Allergan, and payments from our subtenant were our only significant committed potential external sources of funds.

At-the-Market Offering

In March 2017, we entered into a sales agreement with Cowen and Company LLC ("Cowen"), under which we were able from time to time to issue and sell shares of our common stock through Cowen in at-the-market offerings for aggregate gross sales proceeds of $50.0 million. In January 2018, we sold 1,429,205 shares of our common stock to Cowen at a weighted-average price of $34.99 per share for gross proceeds of $50.0 million. We paid a 3% cash commission on the gross sales price per share of common stock sold resulting in us our receiving net proceeds from the offering of approximately $48.5 million. Following these sales, no shares of common stock remained available for sale

under the sales agreement. Shares sold pursuant to the sales agreement were sold pursuant to a shelf registration statement, which became effective on March 15, 2017.

Indebtedness

In December 2016, in connection with our entry into our Cpf1 license agreement with the Broad (the "Cpf1 License Agreement"), we issued promissory notes (the "Initial Notes") in an aggregate original principal amount of $10.0 million to Broad and Wageningen. We fully settled the outstanding principal and accrued interest on the Initial Notes by paying $0.2 million in cash to Wageningen in August 2017 and issuing 108,104 shares and 371,166 shares of common stock to Broad in August 2017 and September 2017, respectively, in connection with such settlement. Upon such issuance and payment, the Initial Notes were cancelled.

In March 2017, a success payment in the amount of $5.0 million under our Cpf1 License Agreement became due upon our market capitalization reaching $750 million, and we issued promissory notes to Broad and Wageningen in the aggregate original principal amount of $5.0 million (the "March Notes"). In August 2017, we issued an aggregate of 271,347 shares of our common stock to Broad and paid $0.4 million to Wageningen as payment of all outstanding principal and interest under the March Notes. Upon such issuance and payment, the March Notes were cancelled. In September 2017, Wageningen designated Broad as the recipient of any future promissory notes that are owed to Wageningen pursuant to the Cpf1 License Agreement.

In December 2017, success payments in the aggregate amount of $7.5 million under our Cpf1 License Agreement and our Cas9-II license agreement with the Broad (the "Cas9-II License Agreement") became due upon our market capitalization reaching $1.0 billion for a specified period of time, and we issued promissory notes to Broad in the aggregate original principal amount of $7.5 million (the "December Notes"). In January 2018, we issued an aggregate of 225,909 shares of our common stock to Broad as payment of all outstanding principal and interest under the December Notes. Upon such issuance, the December Notes were cancelled.

Under the terms of the Cpf1 License Agreement and Cas9-II License Agreement, we may be required to issue additional promissory notes in connection with the achievement of success payment criteria. See Note 8 to our consolidated financial statements 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, 2017, 2016 and 2015, respectively (in thousands):

	Year Ended December 31,		
	2017	2016	2015
Net cash (used in) provided by:			
Operating activities	$ (9,417)	$ (50,246)	$ (5,443)
Investing activities	(183,810)	(3,473)	(1,431)
Financing activities	154,534	97,161	139,391
Net increase (decrease) in cash and cash equivalents	$ (38,693)	$ 43,442	$ 132,517

Net Cash Used in Operating Activities

Net cash used in operating activities was approximately $9.4 million for the year ended December 31, 2017, and consisted primarily of a net loss of $120.3 million adjusted for non-cash items, including stock-based compensation expenses of $23.4 million, non-cash research and development expenses of $14.5 million, depreciation expense of $2.7 million, other non-cash items income of $0.3 million, and a net change in operating assets and liabilities of $70.6 million. The change in operating assets and liabilities was primarily related to an increase in deferred revenue of $81.7 million, primarily related to receiving the Allergan Upfront, partially offset by a decrease of $8.3 million in accrued expenses, a decrease of $1.5 million in accounts payable, an increase in accounts receivable of $0.6 million, and an increase in prepaid expenses and other current assets of $0.6 million

Net cash used in operating activities was $50.2 million for the year ended December 31, 2016, and consisted primarily of a net loss of $97.2 million adjusted for non-cash items, including stock-based compensation expenses of $16.9 million, non-cash research and development expenses of $10.0 million, depreciation expense of $1.2 million, other non-cash items expense of $0.9 million, re-measurement of warrant to purchase redeemable securities of $0.1 million, and a net change in operating assets and liabilities of $17.9 million. The change in operating assets and liabilities was related to an increase in accrued expenses of $11.8 million, an increase in accounts payable of $3.3 million, a decrease in non-current assets of $2.2 million, an increase in deferred revenue of $0.9 million, and a decrease in accounts receivable of $0.9 million, partially offset by an increase in prepaid expenses and other current assets of $1.3 million.

Net cash used in operating activities was $5.4 million for the year ended December 31, 2015, and consisted primarily of a net loss of $72.9 million adjusted for non-cash items, including mark to market of our preferred stock tranche liability, anti-dilutive protection liability, and warrant liability of $37.4 million, stock-based compensation expenses of $3.5 million, depreciation expense of $0.5 million, other non-cash items expense of $0.1 million, and a net change in operating assets and liabilities of $26.0 million. The change in operating assets and liabilities was related to an increase in deferred revenue of $25.3 million, primarily related to receiving the upfront payment under our collaboration agreement with Juno Therapeutics, and an increase in accrued expenses of $3.5 million, partially offset by a decrease in accounts payable of $1.4 million, an increase in accounts receivable of $1.0 million, and an increase in prepaid expenses and other current assets of $0.4 million.

Net Cash Used in Investing Activities

Net cash used in investing activities was approximately $183.8 million for the year ended December 31, 2017, and consisted of expenses to purchase marketable securities of $375.3 million and acquisitions of equipment of $2.1 million, partially offset by proceeds from maturities of marketable securities of $193.5 million.

Net cash used in investing activities was $3.5 million for the year ended December 31, 2016 and consisted primarily of acquisitions of equipment.

Net cash used in investing activities was $1.4 million for the year ended December 31, 2015 and consisted primarily of acquisitions of equipment.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was approximately $154.5 million for the year ended December 31, 2017, primarily related to $154.1 million in proceeds received from public offerings of common stock, net of issuance costs that were paid as of December 31, 2017, and $1.8 million in proceeds from exercises of options for our common stock, partially offset by payments on our construction financing obligation of $0.8 million and payments on our promissory notes of $0.6 million.

Net cash provided by financing activities was approximately $97.2 million for the year ended December 31, 2016 and primarily related to $97.5 million in proceeds received from our IPO, net of issuance costs, and proceeds from exercise of stock options of $0.2 million, partially offset by payments on our construction financing obligation of $0.6 million.

Net cash provided by financing activities was approximately $139.4 million for the year ended December 31, 2015 and primarily consisted of 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, partially offset by payments on our equipment loan of $2.0 million, fees related to our IPO of $1.7 million, and payments of the final fee for our loan payoff of $0.1 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, including reimbursing our licensors for expenses related to the intellectual property that we in-license from such licensors; 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, in 2016 and 2017 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 development programs or future commercialization efforts.

We expect that our existing cash, cash equivalents, and marketable securities at December 31, 2017, anticipated interest income, and anticipated research support under our collaboration agreement with Juno Therapeutics will enable us to fund our operating expenses and capital expenditure requirements for at least the next 24 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 and our strategic alliance with Allergan;
- 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);
- whether Allergan exercises any of its options under our strategic alliance;
- 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 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, 2017 (in thousands):

	Total	Less Than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
Success payment and notes payable[1]	$ 9,500	$ 9,500	$ —	$ —	$ —
Operating lease obligations	25,100	4,055	12,774	8,271	—
Total	$ 34,600	$ 13,555	$ 12,774	$ 8,271	$ —

(1) In January 2018, we issued an aggregate of 80,000 shares of our common stock as payment of the $2.0 million success payment owed to MGH. In January 2018, we issued an aggregate of 225,909 shares of our common stock to the Broad as payment of all outstanding principal and interest under the notes payable in the aggregate original principal amount of $7.5 million and such notes were cancelled.

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—Our Collaborations and Licensing Strategy."

Pursuant to the license agreement with respect to Cas9 that we entered into with Broad and the President and Fellows of Harvard College ("Harvard") in October 2014, as amended and restated in December 2016 and as further amended in March 2017 (the "Cas9-I License Agreement"), the Cpf1 License Agreement, and the Cas9-II License Agreement, we have incurred an aggregate of $18.2 million, $23.1 million, and $9.4 million in expense during the years ended December 31, 2017, 2016 and 2015, 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—Our Collaborations and Licensing Strategy"). 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 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 Cpf1 License Agreement, Broad and Wageningen University ("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 Cpf1 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 Cpf1 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 ("Cpf1 Market Cap Success Payments"), or sale of our company for consideration in excess of those thresholds ("Cpf1 Company Sale Success Payments" and collectively with the Cpf1 Market Cap Success Payments, the "Cpf1 Success Payments"). The Cpf1 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 ("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. As discussed above, we have triggered a total of $12.5 million in success payments under the Cpf1 License Agreement and the Cas9-II License Agreement and the maximum amount payable by us for such success payments described above has been correspondingly reduced.

Under the exclusive patent license agreement we entered into in August 2016 with MGH (the "Second MGH License Agreement"), 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 ("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. In December 2017, an MGH Market Cap Success Payment of $2.0 million became due under our Second MGH License Agreement in connection with our market capitalization reaching $1.0 billion, which we settled in January 2018 through the issuance of 80,000 shares of our common stock to MGH.

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.

We enter into contracts in the normal course of business with contract research organizations 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.

Effects of Inflation

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, 2017, 2016 and 2015.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. As of December 31, 2017, we had cash and cash equivalents of $146.6 million, primarily held in money market mutual funds consisting of U.S. government-backed securities, and marketable securities of $182.5 million, primarily consisting of U.S. government-backed securities. Our

primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments, 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.

While we contract with certain vendors and institutions internationally, substantially all of our total liabilities as of December 31, 2017 were denominated in the United States dollar and we believe that we do not have any material exposure to foreign currency exchange rate risk.

Item 8. Financial Statement and Other Supplementary Information.

EDITAS MEDICINE, INC.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Editas Medicine, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Editas Medicine, Inc. (the Company) as of December 31, 2017 and 2016, and the related consolidated statements of operations, 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, 2017, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the consolidated financial position of the Company at December 31, 2017 and 2016, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2015.
Boston, Massachusetts
March 8, 2018

Editas Medicine, Inc.
Consolidated Balance Sheets
(amounts in thousands, except share and per share data)

	December 31, 2017	December 31, 2016
ASSETS		
Current assets:		
Cash and cash equivalents	$ 146,630	$ 185,323
Marketable securities	182,509	—
Accounts receivable	679	88
Prepaid expenses and other current assets	2,381	1,772
Total current assets	332,199	187,183
Property and equipment, net	39,442	40,378
Restricted cash and other non-current assets	1,619	1,621
Total assets	$ 373,260	$ 229,182
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 4,020	$ 4,640
Accrued expenses	11,049	17,439
Notes payable	7,500	10,000
Deferred revenue, current	13,238	256
Other current liabilities	900	748
Total current liabilities	36,707	33,083
Deferred revenue, net of current portion	94,725	26,000
Construction financing lease obligation, net of current portion	33,431	35,096
Other non-current liabilities	317	396
Total liabilities	165,180	94,575
Commitments and contingencies (see note 8)		
Stockholders' equity		
Preferred stock, $0.0001 par value per share: 5,000,000 shares authorized; no shares issued or outstanding	—	—
Common stock, $0.0001 par value per share: 195,000,000 shares authorized; 45,025,448 and 36,662,724 shares issued, and 44,507,960 and 35,818,131 shares outstanding at December 31, 2017 and December 31, 2016, respectively	4	4
Additional paid-in capital	514,002	320,129
Accumulated other comprehensive loss	(76)	—
Accumulated deficit	(305,850)	(185,526)
Total stockholders' equity	208,080	134,607
Total liabilities and stockholders' equity	$ 373,260	$ 229,182

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

Editas Medicine, Inc.
Consolidated Statements of Operations
(amounts in thousands, except per share and share data)

	Year Ended December 31,		
	2017	2016	2015
Collaboration and other research and development revenues	$ 13,728	$ 6,053	$ 1,629
Operating expenses:			
Research and development	83,159	56,979	18,846
General and administrative	50,502	46,262	18,095
Total operating expenses	133,661	103,241	36,941
Operating loss	(119,933)	(97,188)	(35,312)
Other income (expense), net			
Other income (expense), net	587	(57)	(37,445)
Interest (expense) income, net	(978)	62	(143)
Total other (expense) income, net	(391)	5	(37,588)
Net loss	$ (120,324)	$ (97,183)	$ (72,900)
Reconciliation of net loss to net loss attributable to common stockholders:			
Net loss	$ (120,324)	$ (97,183)	$ (72,900)
Accretion of redeemable convertible preferred stock to redemption value	—	(47)	(394)
Net loss attributable to common stockholders	$ (120,324)	$ (97,230)	$ (73,294)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.98)	$ (3.02)	$ (28.55)
Weighted-average common shares outstanding, basic and diluted	40,323,631	32,219,717	2,566,916

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

Editas Medicine, Inc.
Consolidated Statements of Comprehensive Loss
(amounts in thousands)

	Year Ended December 31,		
	2017	2016	2015
Net Loss	$ (120,324)	$ (97,183)	$ (72,900)
Other comprehensive loss:			
Unrealized loss on marketable securities	(76)	—	—
Comprehensive loss	$ (120,400)	$ (97,183)	$ (72,900)

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)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' (Deficit) Equity
	Shares	Amount	Shares	Amount				
Balance at December 31, 2014	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 thousand	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 $0.3 million	26,666,660	119,722	—	—	—	—	—	—
Accretion of redeemable convertible preferred stock to redemption value	—	394	—	—	(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)
Balance at December 31, 2015	64,817,359	$ 199,915	3,233,638	$ —	$ 5,234	$ (88,348)	$ —	$ (83,114)
Accretion of redeemable convertible preferred stock to redemption value	—	47	—	—	(47)	—	—	(47)
Conversion of redeemable convertible preferred stock into common stock upon closing of the initial public offering	(64,817,359)	(199,962)	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)
Balance at December 31, 2016	—	$ —	35,818,131	$ 4	$ 320,129	$ (185,526)	$ —	$ 134,607
Issuance of common stock from public offering, net of issuance costs of $0.6 million	—	—	4,600,000	—	96,685	—	—	96,685
Issuance of common stock for repayment of notes payable	—	—	750,617	—	14,823	—	—	14,823
Issuance of common stock from public offering, net of issuance costs of $1.7 million	—	—	2,265,500	—	57,223	—	—	57,223
Exercise of stock options	—	—	272,210	—	1,768	—	—	1,768
Vesting of restricted common stock and common stock subject to repurchase	—	—	561,118	—	4,096	—	—	4,096
Vesting of founder shares	—	—	240,384	—	3,989	—	—	3,989
Stock-based compensation expense	—	—	—	—	15,289	—	—	15,289
Unrealized losses on marketable securities	—	—	—	—	—	—	(76)	(76)
Net loss	—	—	—	—	—	(120,324)	—	(120,324)
Balance at December 31, 2017	—	$ —	44,507,960	$ 4	$ 514,002	$ (305,850)	$ (76)	$ 208,080

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

Editas Medicine, Inc.
Consolidated Statements of Cash Flows
(amounts in thousands)

	Year Ended December 31,		
	2017	2016	2015
Cash flow from operating activities			
Net loss	$ (120,324)	$ (97,183)	$ (72,900)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	23,364	16,881	3,513
Depreciation	2,683	1,202	471
Non-cash research and development expenses	14,500	10,000	—
Re-measurement of warrant to purchase redeemable securities	—	87	241
Change in fair value of preferred stock tranche asset or liability	—	—	35,551
Changes in fair value of anti-dilutive protection liability	—	—	1,609
Other non-cash items, net	(300)	869	53
Changes in operating assets and liabilities:			
Accounts receivable	(591)	931	(1,019)
Prepaid expenses and other current assets	(596)	(1,306)	(373)
Other non-current assets	2	2,246	—
Accounts payable	(1,515)	3,251	(1,436)
Accrued expenses	(8,334)	11,841	3,526
Deferred revenue	81,707	935	25,321
Other current and non-current liabilities	(13)	—	—
Net cash used in operating activities	(9,417)	(50,246)	(5,443)
Cash flow from investing activities			
Purchases of property and equipment	(2,059)	(3,493)	(1,431)
Proceeds from the sale of equipment	15	20	—
Purchases of marketable securities	(375,266)	—	—
Proceeds from maturities of marketable securities	193,500	—	—
Net cash used in investing activities	(183,810)	(3,473)	(1,431)
Cash flow from financing activities			
Proceeds from equipment loan, net of issuance costs	—	—	1,500
Proceeds from offering of common stock, net of issuance costs	154,143	97,488	—
Proceeds from exercise of stock options	1,755	233	—
Payments on construction financing lease obligation	(764)	(560)	—
Proceeds from the issuance of redeemable convertible preferred stock and tranche rights, net of issuance costs	—	—	141,711
Payments of notes payable	(600)	—	—
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
Payments of initial public offering costs	—	—	(1,746)
Net cash provided by financing activities	154,534	97,161	139,391
Net increase (decrease) in cash, cash equivalents, and restricted cash	(38,693)	43,442	132,517
Cash, cash equivalents, and restricted cash, beginning of period	186,942	143,500	10,983
Cash, cash equivalents, and restricted cash, end of period	$ 148,249	$ 186,942	$ 143,500
Supplemental disclosure of cash and non-cash activities:			
Accretion of redeemable convertible preferred stock to redemption value	$ —	$ 47	$ 394
Fixed asset additions included in accounts payable and accrued expenses	623	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	11	17
Interest paid	13	465	91
Offering expenses included in accounts payable and accrued expenses	235	—	502
Reclassification of preferred stock tranche liability upon settlement	—	—	37,038
Issuance of common stock for settlement of notes payable	14,823	—	—

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. The Company has primarily financed its operations through various equity and debt financings, including the initial public offering of its common stock (the "IPO"), its follow-on public offerings of its common stock in March 2017 and December 2017, and private placements of preferred stock, from upfront, milestone and research and development fees paid under a research collaboration with Juno Therapeutics, Inc. ("Juno Therapeutics"), and from an upfront payment paid under a strategic alliance and option agreement with Allergan Pharmaceuticals International Limited ("Allergan").

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 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 March 2017, the Company completed a follow-on offering whereby the Company sold 4,600,000 shares of its common stock, inclusive of 600,000 shares of common stock sold by the Company pursuant to the full exercise of an option granted to the underwriters in connection with the offering, at a price to the public of $22.50 per share (the "March Offering"). The aggregate net proceeds received by the Company from the March Offering were $96.7 million, after deducting underwriting discounts and commissions and other offering expenses payable by the Company.

In December 2017, the Company completed a public offering whereby the Company sold 2,265,500 shares of its common stock, inclusive of 295,500 shares of common stock sold by the Company pursuant to the full exercise of an option granted to the underwriter in connection with the offering, at a price to the public of $26.00 per share (the "December Offering"). The aggregate net proceeds received by the Company from the December Offering were $57.2 million, after deducting underwriting discounts and other offering expenses payable by the Company.

The Company has incurred annual net operating losses in every year since its inception. The Company expects that its existing cash, cash equivalents, and marketable securities at December 31, 2017, anticipated interest income, and anticipated research support under the Company's collaboration agreement with Juno Therapeutics will enable it to fund its operating expenses and capital expenditure requirements for at least the next 24 months following the date of this Annual Report on Form 10-K. The Company had an accumulated deficit of $305.9 million at December 31, 2017, and will require substantial additional capital to fund its operations. The Company has never generated any product revenue. 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").

Reclassification

Certain prior period amounts have been reclassified for consistency with the current period presentation. These reclassifications had no effect on previously reported results of operations.

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, deferred tax valuation allowances and sub-license fees due to certain of its licensors. 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 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.

The carrying amounts reflected in the consolidated balance sheets for cash and cash equivalents, restricted cash, marketable securities, accounts receivable, prepaid expenses and other current assets, accounts payable, accrued expenses, and other current liabilities approximate their fair values, due to their short-term nature. The Company believes that the carrying value of the notes payable approximates their fair value based on Level 3 inputs including a quoted rate.

Cash, Cash Equivalents, and Restricted Cash

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 and U.S. government-backed securities.

The Company had restricted cash of $1.6 million, $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, 2017, 2016 and 2015, respectively.

The following table presents cash, cash equivalents, and restricted cash as reported on the consolidated balance sheets that equal the total amounts on the consolidated statements of cash flows (in thousands):

	Year Ended As of December 31,		
	2017	2016	2015
Cash and cash equivalents	$ 146,630	$ 185,323	$ 143,180
Restricted cash included in "Prepaid expenses and other current assets"	—	—	320
Restricted cash included in "Restricted cash and other non-current assets"	1,619	1,619	—
Total	$ 148,249	$ 186,942	$ 143,500

Marketable Securities

The Company classifies marketable securities with a remaining maturity when purchased of greater than three months and less than one year from the balance sheet date as current. Marketable securities with a remaining maturity date greater than one year are classified as non-current. The Company classifies all of its marketable securities as available-for-sale securities. Available-for-sale securities are carried at fair value with the unrealized gains and losses included in other comprehensive loss as a component of stockholders' equity (deficit) until realized. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense over the life of the of the underlying security. Realized gains and losses are included in other income (expense). If any adjustment to fair value reflects a decline in value of the investment, the Company considers all available evidence to evaluate the extent to which the decline is "other-than-temporary." To determine whether an impairment is other-than-temporary, the Company considers whether it has the ability and intent to hold the investment until a market price recovery and considers whether evidence indicating the cost of the investment is recoverable outweighs evidence to the contrary. The Company does not intend to sell the investments and it is not likely that the Company will be required to sell the investments before recovery of their amortized cost bases, which may be maturity.

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 with Juno Therapeutics. 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, 2017 and 2016.

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.

Asset:	Estimated Useful life
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

The Company records certain estimated costs incurred and reported by a landlord as an asset and corresponding financing lease obligation on the consolidated balance sheets. See Note 8, “Commitments and contingencies,” for additional information.

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, 2017.

Revenue Recognition

To date, the Company has primarily earned revenue under the collaboration and license agreement with Juno Therapeutics and the strategic research alliance with Allergan (see Note 9).

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 relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company validates the BESP for units of accounting by evaluating whether changes in the key assumptions used to determine the BESP 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 and in manufacturing preclinical study materials, consultant fees, facility costs including rent, depreciation, and maintenance expenses, and fees for acquiring and maintaining licenses under third party licensing agreements, including any sublicensing or success payments made to the Company's licensors. In accruing service fees, the Company estimates 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 the Company's estimate, the accrual or prepaid is adjusted accordingly. 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.

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 was 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 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 initial public offering, 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 marketable securities, interest expense on the construction financing lease obligation and promissory notes, rental income from the Company's subtenant, interest income, accretion of discounts, and amortization of premiums associated with marketable securities.

Prior to 2017, other income (expense), net consisted 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.

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. Comprehensive loss currently consists of net loss and changes in unrealized losses on marketable securities.

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, cash equivalents, marketable securities and accounts receivable. The Company's cash, cash equivalents and marketable securities 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 (see Note 9) for which the Company does not obtain collateral. As of December 31, 2017, substantially all of the Company's revenue to date has been generated from the strategic alliance with Allergan and the collaboration with Juno Therapeutics.

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.

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, *Revenue Recognition,* 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 entity 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. 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 three revenue arrangements, its license and collaboration with Juno Therapeutics, its award arrangement with the Cystic Fibrosis Foundation Therapeutics, Inc. ("CFFT"), and its strategic alliance with Allergan, pursuant to which it has recognized since inception a total of $12.2 million, $0.3 million, and $8.8 million, respectively, through December 31, 2017. The Company is analyzing the potential impact that ASU 2014-09, ASU 2016-10 and ASU 2016-12 may have on its historical revenue recognition under these three arrangements. This analysis includes, but is not limited to, reviewing variable consideration as it relates to its agreements and in particular, milestone payments as the inclusion of milestone payments in the transaction price could accelerate revenue recognized under ASC 606 compared to ASC 605, evaluating whether a significant financing component is present, determining the revenue recognition method for services performed under the arrangement, and assessing potential disclosures and evaluating the impact of each potential method of adoption on the Company's consolidated financial statements. The Company adopted the new standard effective January 1, 2018 and will use the modified retrospective approach with a cumulative-effect adjustment to retained earnings in the first quarter of 2018. As the Company is still in the process of completing its assessment of its arrangements, an estimate of the potential impact has not yet been made. The Company will complete its assessment in the first quarter of 2018. However, the Company expects the adoption of ASU 2014-09 will have a significant change on the financial statement disclosures.

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 potential impact that the adoption of ASU 2016-02 will have on the Company's consolidated financial statements.

In March 2016, the FASB, issued ASU No. 2016-09, *Compensation - Stock Compensation* ("ASU 2016-09"). ASU 2016-09 simplifies several aspects of the accounting for employee share-based payment transactions, including the accounting for income taxes, forfeitures, and statutory tax withholding requirements, as well as classification in the statement of cash flows. Under this guidance, a company recognizes all excess tax benefits and tax deficiencies as income tax expense or benefit in the income statement as the awards vest or are settled. ASU 2016-09 is effective for public companies for annual reporting periods beginning after December 15, 2016, including interim periods within those annual reporting periods. Upon adoption of this standard on January 1, 2017, the Company recognized previously unrecognized excess tax benefits using the modified retrospective transition method, which resulted in a cumulative-effect increase of $179,000 to deferred tax assets which is offset by a corresponding decrease to the valuation allowance. The implementation of ASU 2016-09 did not have a material impact on stock-based compensation expense. As part of the adoption of ASU 2016-09, the Company elected to record forfeitures as they occur.

In October 2016, the FASB issued ASU No. 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 was effective for fiscal years beginning after December 15, 2017, and interim periods within those years. Early adoption was permitted. The guidance is effective on a retrospective basis. The Company elected to early adopt this guidance as of October 1, 2017. The Company reclassified restricted cash in the statements of cash flows to be included in the cash and cash equivalents balance. The reclassification was not material to the periods presented. See the "Cash, cash equivalents, and restricted cash" section of this note for additional information.

In January 2017, the FASB issued ASU No. 2017-01, *Business Combinations* ("ASU 2017-01"), which clarified the definition of a business and provides a screen to determine when an integrated set of assets and activities is not a business. The screen requires that when substantially all of the fair value of the gross assets acquired, or disposed of, is concentrated in a single identifiable asset or a group of similar identifiable assets, the set is not a business. This new standard was effective for fiscal years beginning after December 15, 2017, and interim periods within those years. Early adoption was permitted. The Company adopted this new standard as of January 1, 2017, with prospective application to any business development transactions.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation-Stock Compensation* ("ASU 2017-09"), which provided guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting. The new guidance requires modification accounting if the vesting condition, fair value or award classification is not the same both before and after a change to the terms and conditions of the award. This new standard was effective for fiscal years beginning after December 15, 2017, and interim periods within those years. Early adoption was permitted. The Company does not anticipate a material impact to its consolidated financial statements as a result of the adoption of this standard.

3. Cash Equivalents & Marketable Securities

Cash equivalents and marketable securities consisted of the following at December 31, 2017 (in thousands):

December 31, 2017	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash equivalents:				
Money market funds	$ 134,635	$ —	$ —	$ 134,635
U.S. Treasuries	11,995	—	—	11,995
Marketable securities:				
U.S. Treasuries	123,606	—	(47)	123,559
Government agency securities	58,979	—	(29)	58,950
Total cash equivalents and marketable securities	$ 329,215	$ —	$ (76)	$ 329,139

Cash equivalents and marketable securities consisted of the following at December 31, 2016 (in thousands):

December 31, 2016	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash equivalents:				
Money market funds	$ 185,323	$ —	$ —	$ 185,323
Total cash equivalents and marketable securities	$ 185,323	$ —	$ —	$ 185,323

At December 31, 2017, the Company held 25 securities that were in an unrealized loss position. The aggregate fair value of securities held by the Company in an unrealized loss position for less than 12 months at December 31, 2017 was $174.0 million, and there were no securities held by the Company in an unrealized loss position for more than 12 months. As of December 31, 2017, the Company did not intend to sell, and would not be more likely than not required to sell, the securities in an unrealized loss position before recovery of their amortized cost bases. Furthermore, the Company has determined that there was no material change in the credit risk of these securities. As a result, the Company determined it did not hold any securities with any other-than-temporary impairment as of December 31, 2017.

There were no realized gains or losses on available-for-sale securities during the year ended December 31, 2017 and 2016.

4. Fair Value Measurements

Assets measured at fair value on a recurring basis as of December 31, 2017 are as follows (in thousands):

Financial Assets	December 31, 2017	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash and cash equivalents				
Money market funds	$ 134,635	$ 134,635	$ —	$ —
U.S. Treasuries	11,995	11,995	—	—
Marketable securities:				
U.S. Treasuries	123,559	123,559	—	—
Government agency securities	58,950	58,950	—	—
Money market funds, included in restricted cash	1,619	1,619	—	—
Total financial assets	$ 330,758	$ 330,758	$ —	$ —

Assets and liabilities measured at fair value on a recurring basis as of December 31, 2016 are as follows (in thousands):

Financial Assets	December 31, 2016	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash and cash equivalents	$ 185,323	$ 185,323	$ —	$ —
Money market funds, included in other current assets	1,619	1,619	—	—
Total financial assets	$ 186,942	$ 186,942	$ —	$ —

There were no transfers between fair value measurement levels during the years ended December 31, 2017 or 2016.

5. Prepaid Expenses and Other Current Assets

Prepaid expense and other current assets consisted of the following (in thousands):

	As of December 31,	
	2017	2016
Prepaid expenses	$ 1,864	$ 1,662
Other	517	110
Total	$ 2,381	$ 1,772

6. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	As of December 31,	
	2017	2016
Building	$ 35,167	$ 35,941
Laboratory equipment	7,415	5,130
Computer equipment	550	392
Leasehold improvements	177	200
Furniture and office equipment	96	170
Software	95	101
Total property and equipment	43,500	41,934
Less: accumulated depreciation	(4,058)	(1,556)
Property and equipment, net	$ 39,442	$ 40,378

The Company recorded $2.7 million, $1.2 million, and $0.5 million in depreciation expense during the years ended December 31, 2017, 2016 and 2015, respectively.

7. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	As of December 31,	
	2017	2016
Employee related expenses	$ 3,708	$ 2,480
Intellectual property and patent related fees	2,370	13,251
Process and platform development expenses	2,301	443
Success payment expenses	2,000	—
Professional service expenses	487	729
Other expenses	183	536
Total	$ 11,049	$ 17,439

8. Commitments and Contingencies

Hurley Street Lease

In February 2016, the Company entered into a lease agreement for 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, 2017 and 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.

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 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
2018	4,055
2019	4,155
2020	4,257
2021	4,362
2022	4,470
2023 and thereafter	3,801
Total minimum lease payments	$ 25,100

Rent expense of approximately $1.2 million, $2.5 million, and $1.0 million was incurred during the years ended December 31, 2017, 2016 and 2015, respectively.

In February 2017, the Company subleased approximately 10,000 square feet of the Hurley Street premises pursuant to a sublease (the "Sublease"). Under the terms of the Sublease, the total minimum rental revenue to be received in the future is $0.4 million as of December 31, 2017. The Sublease commenced in February 2017 and will expire on the eighteen month anniversary thereof, unless it is extended for an additional eighteen month term by the subtenant. If the subtenant elects to extend the term of the lease, the base rent is subject to a minimal increase for the subsequent eighteen month period, which is recorded as other income in the consolidated statements of operations

Licensor Expense Reimbursement

The Company is obligated to reimburse The Broad Institute, Inc. ("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 $18.2 million, $23.1 million, and $9.4 million in expense during the years ended December 31, 2017, 2016 and 2015, respectively, for such reimbursement.

Success Payments

In 2016, the Company entered into patent license agreements with each of 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. The Success Payments are payable, if and when, the Company's market capitalization reaches specified thresholds for a specific period of time or upon a sale of the Company for consideration in excess of those thresholds, as discussed more fully in Note 9 (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 2016 License 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 expense is recorded as a research and development expense in the statements of operations.

The Company triggered the first Success Payment under one of the 2016 License Agreements during the first quarter of 2017 when the Company's market capitalization reached $750 million. On March 28, 2017, the Company issued promissory notes for an aggregate principal amount of $5.0 million to Broad and Wageningen and the Company settled such notes in August 2017.

The Company triggered the second Success Payment under one of the 2016 License Agreements during the fourth quarter of 2017 when the Company's market capitalization reached $1.0 billion. On December 6, 2017, the Company issued promissory notes for an aggregate principal amount of $7.5 million to Broad and the Company settled such notes in January 2018.

The Company triggered the first Success Payment under the MGH license agreement during the fourth quarter of 2017 when the Company's market capitalization reached $1.0 billion (the "First MGH Success Payment"). The Company accrued $2.0 million relating to the First MGH Success Payment owed to MGH which is included in accrued expense on the consolidated balance sheet for the year ended December 31, 2017. The Company settled this liability in shares of common stock in January 2018.

The Broad and Wageningen Success Payments are discussed more fully within the Notes Payable section below.

Notes Payable

In December 2016, in connection with the Company's entry into the Cpf1 license agreement with Broad (the "Cpf1 License Agreement"), one of the 2016 License Agreements, it issued promissory notes in an aggregate principal amount of $10.0 million to Broad and Wageningen (the "Initial Notes"). Outstanding principal and accrued interest on the Initial Notes were due and payable on the earlier of December 2017 or a specified period of time following a Company sale or change of control event. The Initial Notes accrued interest at a rate of 4.8% per annum. The Company fully settled the outstanding principal and accrued interest on the Initial Notes by paying $0.2 million in cash to Wageningen in August 2017 and issuing 108,104 shares and 371,166 shares of common stock to Broad in August 2017 and September 2017, respectively, in connection with such settlement.

In March 2017, a $5.0 million Success Payment under the Cpf1 License Agreement became due upon the market capitalization of the Company's common stock reaching $750 million. The Company issued a promissory note to each of Broad and Wageningen in an aggregate original principal amount of $5.0 million (collectively, the " March Success Payment Notes"). Outstanding principal and accrued interest on the March Success Payment Notes were due and payable in August 2017. The March Success Payment Notes were subject to the same interest and terms as the Initial Notes, other than the maturity date. The Company settled the outstanding principal and accrued interest on the March Success Payment Notes in August 2017 by paying $0.4 million in cash to Wageningen and issuing 271,347 shares of common stock to Broad in August 2017 in connection with the settlement of the March Success Payment Notes. In September 2017, Wageningen designated Broad as the recipient of any future promissory notes that are owed to Wageningen pursuant to the Cpf1 License Agreement.

In December 2017, $7.5 million in Success Payments under the Cpf1 License Agreement and the Cas9-II license agreement with the Broad (the "Cas9-II License Agreement"), one of the 2016 License Agreements, became due

upon the Company's market capitalization reaching $1.0 billion. The Company issued promissory notes to Broad in an aggregate original principal amount of $7.5 million (collectively, the "December Success Payment Notes"). Outstanding principal and accrued interest on the December Success Payment Notes are due and payable in May 2018. The December Success Payment Notes are subject to the same interest and terms as the Initial Notes, other than the maturity date. The December Success Payment Notes were fully settled in shares of common stock in January 2018 (see Note 18).

The Company believes that the carrying value of the December Success Payments 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, 2017 and 2016.

9. 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 the following 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 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 investigational new drug ("IND") application 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 (referred to as 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 ("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 is obligated to pay to the Company an aggregate of up to $22.0 million in research and development funding over the Initial Research Program Term 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 Research Program Term 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 $80.0 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

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. The Company achieved $2.5 million development milestones under the Collaboration Agreement resulting from technical progress in a research program in each of May 2016 (the "First Milestone") and July 2017 (the "Second Milestone"). 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, 2017, the next potential milestone payment that the Company may be entitled to receive under the Collaboration 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* ("ASC 605-25"). 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 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 vendor specific objective evidence of selling price nor third-party evidence 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 BESP. The Company developed the BESP 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 BESP 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 BESP 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 BESP 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

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 BESP was determined to be de minimis. The amounts allocated to each of the development and commercialization licenses are based on the respective BESP 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, 2017, 2016 and 2015, the Company recognized revenue totaling approximately $4.9 million, inclusive of the Second Milestone payment, $5.7 million, inclusive of the First Milestone payment, and $1.6 million, respectively, under the collaboration with Juno Therapeutics.

The revenue is classified as collaboration and other research and development revenue in the accompanying consolidated statement of operations. As of December 31, 2017 and 2016, there was approximately $26.4 million and $26.0 million of deferred revenue related to the Company's collaboration with Juno Therapeutics, respectively, all of which is classified as long-term in the accompanying consolidated balance sheet. In addition, as of December 31, 2017, the Company has recorded accounts receivable of $0.5 million related to reimbursable research and development costs under the Collaboration Agreement for activities performed during the fourth quarter of 2017. There was no receivable balance as of December 31, 2016.

During the years ended December 31, 2017 and 2016, the Company paid $0.5 million and $0.5 million in sublicense fees that were owed to certain of the Company's licensors in connection with the Second Milestone and First Milestone, respectively, which the Company recorded as research and development expenses during such periods.

Allergan Pharmaceuticals Strategic Alliance and Option Agreement

Summary of Agreement

In March 2017, the Company entered into a Strategic Alliance and Option Agreement with Allergan to discover, develop, and commercialize new gene editing medicines for a range of ocular disorders (the "Allergan Agreement"). Over a seven-year research term, Allergan will have an exclusive option to exclusively license from the Company up to five collaboration development programs for the treatment of ocular disorders (each a "CDP"), including the Company's Leber's Congenital Amaurosis type 10 program (the "LCA10 Program").

Under the Allergan Agreement, the Company will use commercially reasonable efforts to develop at least five CDPs and deliver preclinical results and data meeting specified criteria with respect to each CDP (each, an "Option Package" and such criteria, the "Option Package Criteria") to Allergan. The list of proposed targets that may be subject to a CDP may be amended from time to time by mutual agreement of the Company and Allergan. The Company is responsible for the preparation and delivery of a written development plan for each particular CDP setting forth the discovery and research activities to be conducted which is subject to the approval of the alliance steering committee that was formed under the Allergan Agreement, comprised of three members from each of the Company and Allergan (the "Steering Committee"). The Company will maintain primary responsibility for the development efforts under each CDP. The Company is responsible for all research and development costs prior to the achievement of the Option Package Criteria. Upon achievement of the Option Package Criteria, as determined by the Steering Committee, Allergan will have the ability, for a defined period of time ("Initial Option Period") to exercise an option (each, an "Option") to obtain a world-wide right and license to the Company's background intellectual property and the Company's interest in the CDP intellectual property to develop, commercialize, make, have made, use, offer for sale, sell, and import any gene editing therapy product that results from such CDP during the term of the Allergan Agreement (a "Licensed Product") in any category of human diseases and conditions other than the diagnosis, treatment or prevention of any cancer in humans through the use of engineered T-cells and subject to specified other limitations. Allergan has the option to extend the Initial Option Period and require the Company to perform additional research and development services, subject to the payment of additional consideration. After exercise of an Option with respect to a CDP, with the exception of any CDP's where the Company has exercised its profit-sharing option, Allergan will be responsible for all development, manufacturing, and commercialization activities in connection with licensed products arising from such CDP, other than with respect to the LCA10 Program, if LCA10 is designated as a CDP, for which the Company has retained the right to develop that program through the acceptance for filing of the first IND with respect to the LCA10 Program. Upon achievement of IND approval for LCA10, unless the Company has exercised its profit sharing option on LCA10, Allergan will be responsible for all development, manufacturing, and commercialization activities.

The initial term of the Allergan Agreement commenced on March 14, 2017 (the "Effective Date") and continues for seven years ending on March 14, 2024 (the "Research Term"). If the Company has not delivered an Option Package, which includes the results and data from the CDP, for five CDPs that satisfy the Option Package Criteria, then the Research Term will automatically extend by one-year increments until such obligation is satisfied, up to a maximum of ten years from the Effective Date.

The activities under the Allergan Agreement during the Research Term will be governed by the Steering Committee. The Steering Committee will review and monitor the direction of the development plan, evaluate and determine which targets are selected to become CDP, establish the Option Package Criteria for each CDP and evaluate the achievement of such criteria as well as oversee the development and commercialization activities after Allergan has licensed a CDP.

Under the terms of the Allergan Agreement, the Company received a $90.0 million up-front, non-refundable, non-creditable cash payment (the "Allergan Upfront") related to the Company's research and development costs for Option Packages for at least five CDPs and for reimbursement of the Company's past out of pocket costs with respect to the prosecution and defense of patents that it owns and in-licenses. Allergan has the option to purchase at least five development and commercialization licenses associated CDP that have satisfied the Option Package Criteria. The option exercise fee during the Initial Option Period is $15.0 million per CDP. If Allergan elects to extend the Initial Option

Period, Allergan is required to pay an additional fee of $5.0 million to extend the option, at which point the Company is required to perform additional research services. If Allergan elects to exercise its option to a development and commercialization license after extending the Initial Option Period, Allergan must pay the Company the option exercise fee of $22.5 million, plus specified costs incurred by the Company in connection with the additional development work.

Following the exercise by Allergan of an Option with respect to a CDP, Allergan would be required to make certain milestone payments to the Company upon the achievement of specified development, product approval and launch and commercial events, on a CDP by CDP basis. On a CDP by CDP basis, for the first product in the first field to achieve the associated event, the Company is eligible to receive up to an aggregate of $42.0 million for development milestone payments and $75.0 million for product approval and launch milestone payments, in each case, for an indication in the field per CDP. In addition, the Company is eligible to receive additional development and product approval and launch milestone payments for subsequent products developed within two additional fields. The Company is also eligible for up to $90.0 million in sales milestone payments on a CDP by CDP basis, associated with aggregate worldwide sales. Certain product approval milestones are subject to certain reductions under specified circumstances, including for payments required to be made by Allergan to obtain certain third party intellectual property rights. In addition, within 45 days of the acceptance by the applicable regulatory authority of the Company's submission of an IND application with respect to the LCA10 Program, Allergan is required to pay the Company a one-time payment of $25.0 million (the "LCA10 IND Payment"), whether or not Allergan exercises its option under the Allergan Agreement to acquire an exclusive license with respect to the LCA10 Program. As of December 31, 2017, the next potential milestone payment that the Company may be entitled to receive under the Allergan Agreement is a substantive milestone payment of $8.0 million for the achievement of certain clinical criteria.

With respect to the LCA10 Program and up to one other CDP of the Company's choosing, following the exercise by Allergan of its Option to such programs, the Company will have the right to elect to participate in a profit-sharing arrangement with Allergan in the United States, on terms mutually agreed by the Company and Allergan and subject to a right of Allergan to reject such election under certain circumstances, under which the Company and Allergan would share equally in net profits and losses on specific terms to be agreed between the Company and Allergan, in lieu of Allergan paying royalties on net sales of any applicable Licensed Products in the United States, and in such event Allergan's milestone payment obligations would be reduced, with the Company being eligible to receive development and product approval and launch milestone payments up to a low nine-digit amount in the aggregate and further sales milestone payments up to a high-eight digit amount in the aggregate, subject to reduction under certain circumstances. If the Company elects to participate in a profit-sharing arrangement, the Company is obligated to reimburse Allergan for half of the development costs incurred by Allergan with respect to the applicable CDP, and Allergan will retain control of all development and commercialization activities for the applicable Licensed Products.

In addition, to the extent there is any Licensed Product, the Company would be entitled to receive tiered royalty payments of high single digits based on a percentage of net sales of such Licensed Product, subject to certain reductions under specified circumstances, and the Company will remain obligated to pay all license fees, milestone payments, and royalties due to its upstream licensors based on Allergan's exercise of its license rights with respect to Licensed Products. However, if a Licensed Product is subject to a profit sharing agreement the royalties will only be paid on ex-US net sales. 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 Licensed Product in a country until the later of: (i) the tenth anniversary of the first commercial sale of such Licensed Product in such country (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 and (iii) the expiration of an exclusive legal right granted by the regulatory authority in such country to market and sell such Licensed Product.

Unless earlier terminated, the Allergan Agreement will terminate upon (i) the expiration of the Research Term, if Allergan does not exercise an Option, (ii) on a Licensed Product-by-Licensed Product and country-by-country basis, on the date of the expiration of all payment obligations under the Allergan Agreement with respect to such Licensed Product in such country or (iii) in its entirety upon the expiration of all payment obligations with respect to the last Licensed Product in all countries, unless terminated earlier due to the early termination provisions. Either party may terminate the Allergan 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. During the Research Term, Allergan will have the right to terminate the Allergan Agreement on a CDP by CDP basis in the event of a change in

control of the Company or for all CDPs, provided that Allergan will not have any right to exercise an Option for any CDPs following such termination. After the exercise of an Option, Allergan will have the right, at its sole discretion, to terminate the Allergan Agreement, on a CDP by CDP basis, upon 90 days' written notice. The Company may terminate the Allergan Agreement in the event that Allergan 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. Lastly, Allergan may terminate the Allergan Agreement with respect to a CDP if a safety concern, as specified in the Allergan Agreement, arises.

Termination of the Allergan Agreement for any reason will 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. In addition, termination of the Allergan Agreement will not 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 Allergan Agreement. If Allergan terminates the Allergan Agreement as a result of the Company's uncured material breach or default, then: (i) the licenses and rights conveyed to Allergan will continue as set forth in the agreement for any CDP Allergan has already licensed and (ii) Allergan's obligations related to milestones and royalties will continue as set forth in the agreement. If the Allergan Agreement is terminated for any other reason, then the options and licenses conveyed to Allergan under the agreement will terminate.

Accounting Analysis

The Company evaluated the Allergan Agreement in accordance with the provisions of ASC 605-25. The Company's arrangement with Allergan contains the following deliverables: (i) research and development services during the Research Term (the "Allergan R&D Services Deliverable"), and (ii) ASC services during the Research Term (the "ASC Deliverable").

The Company has determined that the Options with respect to the CDP are substantive options. Allergan is not contractually obligated to exercise the Options and as a result of the uncertain outcome of the discovery, research and development activities as well as the significant option exercise fee payable upon exercise of an Option, there is significant uncertainty as to whether Allergan will decide to exercise its Option for any CDP. Consequently, the Company is at risk with regard to whether Allergan will exercise the Options. In addition, the option exercise fees are not priced at a significant and incremental discount. Accordingly, the substantive options are not considered deliverables at the inception of the arrangement and the associated option exercise payments are not included in allocable arrangement consideration. The Company has also determined that any obligations which are contingent upon the exercise of a substantive option are not considered deliverables at the outset of the arrangement.

The Company has concluded that the services being provided as part of the ASC Deliverable does not qualify for separation from the Allergan R&D Services Deliverable. The Steering Committee provides oversight and management of the overall Allergan Agreement, and the members of the Steering Committee from the Company have specialized industry knowledge, particularly as it relates to genome editing technology. The Company has concluded that the Steering Committee is a participatory obligation of the Company and is meant to facilitate the early stage research being performed and coordinate the activities of both the Company and Allergan. Further, the Steering Committee services are critical to the selection of the CDP, the ongoing evaluation of the CDP and the development and evaluation of the Option Package Criteria. Accordingly, the Company's participation on the Steering Committee is essential to Allergan receiving value from the Allergan R&D Services Deliverable and as such, the ASC Deliverable along with the Allergan R&D Services Deliverable are considered one unit (the "CDP Services Unit"). As the Company concluded that the CDP Services Unit is the sole unit of accounting (the "CDP Services Unit of Accounting"), all of the initial arrangement consideration will be allocated to that unit and no allocation of arrangement consideration is necessary.

Allocable arrangement consideration at inception is comprised solely of the up-front payment of $90.0 million. The Company will recognize revenue related to the CDP Services Unit of Accounting as the underlying services are performed. In addition, as the LCA10 IND Payment is payable upon acceptance of the IND, it is contingent consideration related to the licensed technology. As such, if and when the LCA10 IND Payment is received, the Company will recognize revenue related to the LCA10 IND Payment in conjunction with the CDP Services Unit of Accounting as the underlying services are performed.

The Company has evaluated all of the milestones that may be received in connection with the Allergan Agreement. 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 product approval and launch milestones are considered substantive on the basis of the contingent nature of the milestones, specifically reviewing factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the milestone. 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 sales 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, 2017, the Company recognized revenue totaling approximately $8.8 million with respect to the Allergan Agreement. As of December 31, 2017, there was $81.2 million of deferred revenue related to the Allergan Agreement, of which $68.3 million is classified as long-term on the consolidated balance sheet. The Company will recognize revenue on a straight-line basis, as there is no discernible pattern or objective measure of performance of the services, over the estimated performance period. The estimated performance period is from the commencement of providing services related to the CDP Services Unit until the end of the Research Term.

During the year ended December 31, 2017, the Company paid $14.1 million in sublicense fees that were owed to certain of the Company's licensors in connection with the Allergan Upfront, which the Company recorded as research and development expenses during such period.

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 (i.e. anti-dilution protection liability), which was settled in June 2015. MGH is entitled to receive nominal annual license fees and future clinical, regulatory and commercial milestone payments in an aggregate maximum amount of $3.7 million and an aggregate amount 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 sublicenses. 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 2016. 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 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 meeting or exceeding $1.0 billion, 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 Company triggered the first Success Payment under the MGH license agreement during the fourth quarter of 2017 when the Company's market capitalization reached $1.0 billion (see Note 8).

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, the 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.

In December 2016, the Company entered into the Cpf1 License Agreement with Broad, for specified patent rights (the "Cpf1 Patent Rights") related primarily to Cpf1 compositions of matter and their use for gene editing. Concurrently with entering into the Cpf1 License Agreement, the Company, Broad, and Harvard amended and restated the Cas9-I License Agreement as described below. Concurrently, the Company and Broad also entered into 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 paid an upfront fee in aggregate of $16.5 million, which included the Initial Notes, under these agreements which was recorded in research and development expenses during 2016.

Cpf1 License Agreement

Pursuant to the Cpf1 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 "Cpf1 Institutions") granted the Company an exclusive, worldwide, royalty-bearing, sublicensable license to the Cpf1 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 "Cpf1 Exclusive Field"), as well as a non-exclusive, worldwide, royalty-bearing sublicensable license to the Cpf1 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 Cpf1 Exclusive Field. The Company is also required to achieve certain development milestones within specified time periods for products covered by the Cpf1 Patent Rights, with Broad having the right to terminate the Cpf1 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 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 Cpf1 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 Cpf1 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 Cpf1 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 Cpf1 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 "Cpf1 Market Cap Success Payments") or a Company sale for consideration in excess of those thresholds (the "Cpf1 Company Sale Success

Payments" and, collectively with the Cpf1 Market Cap Success Payments, the "Cpf1 Success Payments"). The Cpf1 Success Payments payable to Broad and Wageningen are triggered when the Company's market capitalization reaches certain amounts ranging from $750 million to $10 billion for a specified period of time, and, collectively, the Cpf1 Success Payments will not exceed, in aggregate, $125.0 million, which maximum amount 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 Cpf1 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 Cpf1 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 Initial Notes, as described in Note 8, 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, Cpf1 Market Cap Success Payments are required to be made in cash. Cpf1 Company Sale Success Payments are payable solely in cash. The Company triggered the first and second Cpf1 Success Payments during 2017 when the Company's market capitalization reached $750 million and $1.0 billion, respectively (see Note 8).

Unless terminated earlier, the term of the Cpf1 License Agreement will expire on a country-by-country basis, upon the expiration of the last to expire valid claim of the Cpf1 Patent Rights in such country. The Company has the right to terminate the Cpf1 License Agreement at will upon four months' written notice to Broad. Either party may terminate the Cpf1 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 Cpf1 License Agreement immediately if the Company challenges the enforceability, validity, or scope of any Cpf1 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 Cas9-I License Agreement

In December 2016, the Company amended and restated the Cas9-I License Agreement (such agreement, as amended, the "Amended and Restated 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 one third party at a time with respect to each such target within the field of the 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 Cpf1 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 Cpf1 License Agreement or the Cas9-II Agreement. In March 2017, the Company and Harvard and Broad further amended the Amended and Restated Cas9-I License Agreement to (i) grant an exclusive license from Broad to the Company with respect to certain patent rights that The Rockefeller University ("Rockefeller") has or may have rights in and to and for which Rockefeller has, under a certain inter-institutional agreement that Broad and Rockefeller entered into in February 2017, appointed Broad as sole and exclusive agent for the purposes of licensing and (ii) provide to Rockefeller certain rights, including with respect to patent enforcement, indemnification, insurance, confidentiality, reservation of certain rights, and publicity, that are generally consistent with those granted to Broad, Harvard, MIT and the Howard Hughes Medical Institute under the Amended and Restated Cas9-I License Agreement, as amended.

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 the Cpf1 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 digit dollar amount and will have to pay 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 sales milestone payments for any such licensed product totaling up to $13.5 million in the aggregate. In addition, the Company is obligated 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. Consistent with the Cpf1 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 $1.0 billion to $9.0 billion or upon a sale of the Company for consideration in excess of those thresholds. 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 amount 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. The Company triggered the first success payment during the fourth quarter of 2017 when the Company's market capitalization reached $1.0 billion, which the Company settled in January 2018 (see Note 8).

10. 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 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, 2017, the Company had no shares of preferred stock issued or outstanding.

11. 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, 2017:

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,	
	2017	2016
Shares reserved for outstanding stock option awards under the 2013 Stock Incentive Plan, as amended	1,220,567	1,595,082
Shares reserved for outstanding stock option awards under the 2015 Stock Incentive Plan	2,921,987	1,569,746
Shares reserved for outstanding inducement stock option award	225,000	—
Remaining shares reserved, but unissued, for future awards under the 2015 Stock Incentive Plan	2,502,338	2,760,472
Remaining shares reserved, but unissued, for future awards under the 2015 Employee Stock Purchase Plan	751,242	384,615
	7,621,134	6,309,915

March 2017 Common Stock Sales Agreement

In March 2017, the Company entered into a sales agreement with Cowen and Company LLC ("Cowen), under which the Company from time to time can issue and sell shares of its common stock through Cowen in at-the-market offerings ("March 2017 ATM Program") for aggregate sales proceeds of $50.0 million. The common stock will be distributed at the market prices prevailing at the time of sale. All sales of shares will be made pursuant to an effective shelf registration statement on Form S-3 filed with the SEC. The Company will pay Cowen a commission of 3% of the aggregate gross proceeds the Company receives from all sales of the Company's common stock under the sales agreement. As of December 31, 2017, the Company had not received any proceeds under the March 2017 ATM Program. Subsequent to December 31, 2017 and during January 2018, the Company sold an aggregate of 1,429,205 common shares under the March 2017 ATM Program at an average price of $34.99 per common share for gross proceeds of $50.0 million.

12. 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.

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 in the applicable options. Awards granted to non-employee consultants generally vest monthly over a period of one to four years. In connection with the IPO, the Company's board of directors determined to grant no further awards 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 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. 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. On January 1, 2018, the Company increased the shares under the 2015 Plan by 1,801,017 shares.

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 IPO. 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 first offering under the 2015 ESPP opened on December 1, 2017. On January 1, 2018, the Company increased the shares under the 2015 ESPP Plan by 450,254 shares.

Founder Awards

In September 2013, the Company issued 2,403,845 shares of restricted stock to its non-employee founders for services rendered subject to certain repurchase rights. 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 were subject to repurchase rights. Accordingly, the Company recorded the proceeds from the issuance of restricted stock as a liability in its consolidated balance sheets. The restricted stock liability was reclassified into stockholders' equity (deficit) as the restricted stock vested. 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. The remaining founder awards completed vesting in August 2017.

Stock-based compensation expense associated with these awards was recognized as the awards vested. Unvested awards were 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 was as follows (in thousands):

	Year Ended December 31,		
	2017	2016	2015
Research and development	$ 15,131	$ 4,234	$ 3,015
General and administrative	8,233	12,647	498
Total stock-compensation expense	$ 23,364	$ 16,881	$ 3,513

Restricted Stock

From time to time, upon approval by the Company's 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. 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, 2016 and 2017 is as follows:

	Shares	Weighted Average Grant Date Fair Value Per Share
Unvested Restricted Common Stock as of December 31, 2016	822,638	$ 0.02
Issued	480,000	$ 28.05
Vested	(784,119)	$ 4.95
Forfeited	(5,294)	$ 0.03
Unvested Restricted Common Stock as of December 31, 2017	513,225	$ 18.70

The expense related to restricted stock awards granted to employees and non-employees was $0.5 million and $4.1 million, respectively, for the year ended December 31, 2017. 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, 2017, the Company had no unrecognized stock-based compensation expense related to its employee unvested restricted stock awards. As of December 31, 2017, the Company had unrecognized stock-based compensation expense related to its non-employee unvested restricted stock awards of $10.3 million which is expected to be recognized over a remaining weighted average vesting period of 4.7 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. The liability for unvested common stock subject to repurchase is reclassified into stockholders' equity (deficit) as the shares vest.

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

	Shares	Weighted Average Exercise Price	Remaining Contractual Life	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2016	3,411,783	$ 13.71	8.8	$ 16,190
Granted	1,392,689	—	—	—
Exercised	(289,583)	—	—	—
Cancelled	(142,753)	—	—	—
Outstanding at December 31, 2017	4,372,136	$ 17.28	8.5	$ 60,591
Vested and expected to vest at December 31, 2017	4,372,126	$ 17.28	8.5	$ 60,591
Exercisable at December 31, 2017	1,540,023	$ 14.95	8.3	$ 25,099

The table above reflects unvested stock options as exercised on the dates that the shares are no longer subject to repurchase. The Company had 4,572 and 21,955 shares of unvested common stock at December 31, 2017 and 2016 related to the exercise of unvested stock options.

The total intrinsic value of options exercised for the years ended December 31, 2017, 2016, and 2015 was $5.0 million, $0.9 million, and $0.1 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, 2017, 2016, and 2015 was $16.07, $14.10, and $5.91, respectively. The expense related to options granted to employees and directors was $12.3 million, $6.0 million, and $0.7 million for the years ended December 31, 2017, 2016, and 2015, respectively.

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,		
	2017	2016	2015
Expected volatility	77.8 %	78.4 %	78.8 %
Expected term (in years)	6.25	6.25	6.25
Risk free interest rate	2.1 %	1.5 %	1.7 %
Expected dividend yield	—	—	—

There were no options granted to persons other than employees and directors during the year ended December 31, 2017. For the year ended December 31, 2017, 2016 and 2015, 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,		
	2017	2016	2015
Expected volatility	—	76.5 %	80.0 %
Expected term (in years)	—	10.0	10.0
Risk free interest rate	—	1.6 %	2.2 %
Expected dividend yield	—	—	—

As of December 31, 2017, the Company had unrecognized stock-based compensation expense related to its employee stock options of $33.4 million which the Company expects to recognize over a remaining weighted average vesting period of 2.5 years.

13. 401(k) Savings Plan

The Company has a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code of 1986, as amended (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 made $0.5 million in contributions to the 401(k) Plan for the year ended December 31, 2017 and did not make any contributions for the years ended December 31, 2016 and 2015, respectively.

14. 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,		
	2017	2016	2015
Income tax computed at federal statutory tax rate	34.0 %	34.0 %	34.0 %
State taxes, net of federal benefit	5.9 %	3.5 %	2.5 %
General business credit carryovers	2.5 %	1.5 %	0.8 %
Non-deductible expenses	(2.1)%	(3.6)%	(17.9)%
Federal tax rate reduction	(24.7)%	— %	— %
Change in valuation allowance	(15.6)%	(35.4)%	(19.4)%
	— %	— %	— %

On December 22, 2017, legislation commonly known as the Tax Cuts and Jobs Act (the "Tax Act") was signed into law. The Tax Act, among other changes, reduces the U.S. federal corporate tax rate from 34% to 21%, requires taxpayers to pay a one-time transition tax on earnings of certain foreign subsidiaries that were previously tax deferred and creates new taxes on certain foreign sourced earnings. As of December 31, 2017, the Company did not have any foreign subsidiaries and the international aspects of the Tax Act are not applicable.

In connection with the initial analysis on the impact of the Tax Act, the Company remeasured certain deferred tax assets and liabilities based on the rates at which they are expected to reverse in the future, which is generally 21%. The remeasurement of the Company's deferred tax balance was primarily offset by application of its valuation allowance. However, the reduction of the U.S. federal corporate tax rate resulted in increases to the amounts reflected in "Federal tax rate reduction" and "Change in valuation allowance" captions for the year ended December 31, 2017 in the Company's tax reconciliation table compared to those amounts disclosed for the years ended December 31, 2016 and 2015. The change in the U.S. federal corporate tax rate, which is effective January 1, 2018, is also reflected in the Company's deferred tax table.

The Company is still in the process of analyzing the impact to the Company of the Tax Act. On December 22, 2017, the SEC staff issued SAB 118 to address the application of GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Tax Act. The Company has recognized the provisional tax impacts related to the revaluation of the deferred tax assets and liabilities and included these amounts in its consolidated financial statements for the year ended December 31, 2017. The ultimate impact may differ from these provisional amounts due to, among other things, additional analysis, changes in interpretations and assumptions the Company has made, additional regulatory guidance that may be issued, and actions the Company may take as a result of the Tax Act, which could result in changes to the provisional tax impacts during 2018.

The principal components of the Company's deferred tax assets and liabilities consist of the following at December 31, 2017 and 2016 (in thousands):

	Year Ended December 31,	
	2017	2016
Deferred tax assets:		
Net operating loss carryforwards	$ 27,726	$ 16,490
Tax credit carryforwards	5,259	2,014
Accrued expenses	2,079	7,353
Capitalized patent costs	26,307	16,025
Deferred revenue	7,151	9,672
Construction financing lease obligation	9,352	13,685
Other	4,978	2,979
Total deferred tax assets	82,852	68,218
Less valuation allowance	(73,301)	(54,300)
Net deferred tax assets	9,551	13,918
Deferred tax liabilities—depreciation and amortization	(9,551)	(13,918)
Net deferred taxes	$ —	$ —

The Company has incurred net operating losses ("NOL") since inception. At December 31, 2017 and 2016, the Company had federal and state net operating loss carryforwards of $202.7 million and $82.4 million respectively, which expire beginning in 2033 and will continue to expire through 2037. As of December 31, 2017 and 2016, the Company had federal and state research and development tax credits carryforwards of $5.6 million and $2.3 million, respectively, which expire beginning in 2028 and will continue to expire through 2037.

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, research and development credit carryforwards and capitalized license and patent costs. 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 $73.3 million and $54.3 million has been established at December 31, 2017 and 2016, respectively. The increase in the valuation allowance of $19.0 million for the year ended December 31, 2017 was primarily due to current year operating losses offset by the federal rate reduction from 34% to 21% as a result of the Tax Act.

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 taken 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, 2017 and 2016, 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, 2017. There are no federal or state audits in process.

15. 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 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.

Upon the closings of the March Offering and the December Offering, the Company sold 4,600,000 and 2,265,500 shares of common stock, respectively. The issuance of these shares resulted in a significant increase in the Company's weighted-average shares outstanding for the year ended December 31, 2017 when compared to the comparable prior year period 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 and twelve 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,	
	2017	2016
Unvested restricted common stock	513,225	822,638
Outstanding stock options	4,372,126	3,411,783
Estimated number of shares issuable for convertible notes [1]	244,896	—
Total	5,130,247	4,234,421

(1) Represents the number of shares that would have been issued if the Company had elected to pay the December Success Payment Notes, as discussed in Note 8, in shares of the Company's common stock, based on the closing price of the common stock on December 31, 2017. The number of shares issued, for purposes of this presentation, is calculated by dividing the principal of the notes payable, including accrued interest, by the stock price per share.

The table above reflects restricted stock issued upon exercise of unvested stock options as exercised on the dates that the shares are no longer subject to repurchase.

16. Related-Party Transactions

During the years ended December 31, 2016 and December 31, 2015, the Company paid a related party $1.4 million and $1.2 million in rent and facility-related fees, respectively. The Company did not make any payments to this related party during the year ended December 31, 2017. The Company received $0.8 million in rent and facility-related fees from a related party during the year ended December 31, 2017 in connection with the Sublease; no rent or facility-related payments were received from this related party during the year ended December 31, 2016 or December 31, 2015. In addition, during the year ended December 31, 2015, the Company paid one of its investors $0.1 million in professional fees.

17. Selected Quarterly Financial Data (unaudited) –

The following table contains selected quarterly financial information from 2017 and 2016. 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, 2017	June 30, 2017	September 30, 2017	December 31, 2017
	(in thousands, except per share data)			
Total revenue	$ 682	$ 3,097	$ 6,282	$ 3,667
Total operating expenses	31,309	29,212	33,031	40,109
Total other income (expense), net	(470)	(324)	150	253
Net loss	$ (31,097)	$ (26,439)	$ (26,599)	$ (36,189)
Net loss applicable to common stockholders	$ (31,097)	$ (26,439)	$ (26,599)	$ (36,189)
Net loss per share applicable to common stockholders — basic and diluted	$ (0.85)	$ (0.65)	$ (0.64)	$ (0.84)

	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 income (expense), net	94	158	145	(392)
Net loss	$ (17,745)	$ (19,042)	$ (21,020)	$ (39,376)
Net loss applicable to common stockholders	$ (17,792)	$ (19,042)	$ (21,020)	$ (39,376)
Net loss per share applicable to common stockholders — basic and diluted	$ (0.80)	$ (0.54)	$ (0.59)	$ (1.10)

18. Subsequent Events

In January 2018, the Company issued an aggregate of 225,909 shares of its common stock to Broad as payment of all outstanding principal and interest under the December Success Payment Notes (see Note 8). Upon such issuance and payment, the December Success Payment Notes were cancelled.

In January 2018, the Company issued an aggregate of 80,000 shares of its common stock to MGH in connection with settling the First MGH Success Payment (see Note 8).

In January 2018, the Company paid $1.6 million in cash and issued an aggregate of 56,099 shares of its common stock, valued at $29.76 per share, to i2 Pharmaceuticals, Inc. in connection with the purchase of certain assets pursuant to an asset purchase agreement.

In January 2018, the Company sold an aggregate of 1,429,205 common shares under the March 2017 ATM Program at an average price of $34.99 per common share for gross proceeds of $50.0 million. The March 2017 ATM Program was fully utilized in January 2018.

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, 2017. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934 (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, 2017, 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, 2017.

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, 2017 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.

Except to the extent provided below, the information required by this Item 10 will be included in the section captioned "Corporate Governance" and the subsections thereof, "Nominees for Election as Class II Directors," "Directors Continuing in Office," "Executive Officers Who Are Not Directors," "Section 16(a) Beneficial Ownership Reporting Compliance," in our definitive proxy statement to be filed with the Securities and Exchange Commission ("SEC") with respect to our 2018 Annual Meeting of Stockholders, which information is incorporated herein by reference.

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. 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. We will provide any person, without charge, a copy of such Code of Business Conduct and Ethics upon written request, which may be mailed to 11 Hurley Street, Cambridge, MA 02141, Attn: Corporate Secretary.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in the section captioned "Executive and Director Compensation" in our definitive proxy statement to be filed with the SEC with respect to our 2018 Annual Meeting of Stockholders, which information is incorporated herein by reference.

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

The information required by this Item 12 will be included in the sections captioned "Principal Stockholders" and "Securities Authorized for Issuance under Equity Compensation Plans" in our definitive proxy statement to be filed with the SEC with respect to our 2018 Annual Meeting of Stockholders, which information is incorporated herein by reference.

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

The information required by this Item 13 will be included in the sections captioned "Transactions with Related Persons" and "Director Independence" in our definitive proxy statement to be filed with the SEC with respect to our 2018 Annual Meeting of Stockholders, which information is incorporated herein by reference. On March 7, 2018, we terminated our Amended and Restated Investors' Rights Agreement, dated as of August 4, 2015 (the "Investors' Rights Agreement"), by and between us and holders of our previously-outstanding preferred stock (the "Holders"). The Investors' Rights Agreement had provided the Holders with the right, subject to certain conditions, to register shares of common stock issued upon conversion of such Holders preferred stock upon a demand request or in connection with our registration of shares for our own account. The termination was effected pursuant to the termination provision of the Investors' Rights Agreement with the consent of all the Holders holding shares that remained subject to the Investors' Rights Agreement, including Katrine S. Bosley, our Chief Executive Officer, and Boris Nikolic, a member of the Board of Directors.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be included in the sections captioned "Audit Fees" and "Audit Committee Pre-Approval Policies and Procedures" in our definitive proxy statement to be filed with the SEC with respect to our 2018 Annual Meeting of Stockholders, which information is incorporated herein by reference.

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 following Exhibit Index.

EXHIBIT INDEX

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File No.	Date of Filing	Exhibit Number	
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+	2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.5	
10.2+	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.6	
10.3+	Form of Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.7	
10.4+	Form of Early Exercise Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.8	
10.5+	Form of Restricted Stock Agreement under 2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.9	
10.6+	2015 Stock Incentive Plan	S-1	333-208856	1/4/2016	10.10	
10.7+	Form of Incentive Stock Option Agreement under 2015 Stock Incentive Plan	S-1	333-208856	1/4/2016	10.11	
10.8+	Form of Nonstatutory Stock Option Agreement under 2015 Stock Incentive Plan	S-1	333-208856	1/4/2016	10.12	
10.9+	Form of Restricted Stock Agreement under 2015 Stock Incentive Plan	10-Q	001-37687	11/8/2017	10.1	
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.	10-K	001-37687	3/3/2017	10.11	
10.12+	Employment Offer Letter, dated July 19, 2016, between the Registrant and Gerald Cox, M.D., Ph.D.	10-K	001-37687	3/3/2017	10.11	
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	10-K	001-37687	3/3/2017	10.16
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†	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
10.19	Amendment No.1 to Amended and Restated Cas9-I License Agreement, by and among Editas Medicine, Inc., President and Fellows of Harvard College, and the Broad Institute, Inc., dated March 3, 2017	8-K	001-37687	3/7/2017	99.1
10.20†	License and Collaboration Agreement, dated May 26, 2015, between the Registrant and Juno Therapeutics, Inc.	S-1	333-208856	1/4/2016	10.23
10.21+	Summary of Director Compensation Program	S-1	333-208856	1/4/2016	10.24
10.22+	2015 Employee Stock Purchase Plan	S-1	333-208856	1/4/2016	10.25
10.23+	Severance Benefits Plan	S-1	333-208856	1/4/2016	10.27
10.24	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers	S-1	333-208856	1/4/2016	10.28
10.25	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
10.26†	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
10.27†	Cpf1 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
10.28†	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
10.29†	Strategic Alliance and Option Agreement, dated March 14, 2017, by and between the Registrant and Allergan Pharmaceuticals International Limited	10-Q	001-37687	5/15/2017	10.1
10.30	Common Stock Sales Agreement, dated March 3, 2017, between the Registrant and Cowen and Company, LLC	S-3	333-216444	3/3/2017	1.2
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

† Confidential treatment has been granted as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.
+ Management contract or compensatory plan or arrangement.

Item 16. Form 10-K Summary.
None.

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 8, 2018

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.

Signature	Title	Date
/s/ Katrine S. Bosley Katrine S. Bosley	President and Chief Executive Officer, Director (principal executive officer)	March 8, 2018
/s/ Andrew A. F. Hack Andrew A.F. Hack, M.D., Ph.D.	Chief Financial Officer (principal financial and accounting officer)	March 8, 2018
/s/ Kevin Bitterman Kevin Bitterman, Ph.D.	Director	March 8, 2018
/s/ Alexis Borisy Alexis Borisy	Director	March 8, 2018
/s/ Andrew Hirsch Andrew Hirsch	Director	March 8, 2018
/s/ Jessica Hopfield Jessica Hopfield, Ph.D.	Director	March 8, 2018
/s/ John D. Mendlein John D. Mendlein, Ph.D., J.D.	Director	March 8, 2018
/s/ Boris Nikolic Boris Nikolic, M.D.	Director	March 8, 2018
/s/ Akshay K. Vaishnaw Akshay K. Vaishnaw, M.D., Ph.D.	Director	March 8, 2018

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements (Form S-3 Nos. 333-216444, 333-216528, 333-222266 and Form S-8 pertaining to the 2013 Stock Incentive Plan, the 2015 Stock Incentive Plan and 2015 Employee Stock Purchase Plan of Editas Medicine, Inc. of our report dated March 8, 2018, with respect to the consolidated financial statements of Editas Medicine, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2017.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 8, 2018

Exhibit 31.1

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; and

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 8, 2018

By: /s/ Katrine S. Bosley
Katrine S. Bosley
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

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; and

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 8, 2018

By: /s/ Andrew A. F. Hack
Andrew A. F. Hack, M.D., Ph.D.
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

**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, 2017, 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 8, 2018

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