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, 2018

or

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

Commission File Number 001-37687

EDITAS MEDICINE, INC.

(Exact name of registrant as specified in its charter)

Delaware	**46-4097528**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
11 Hurley Street **Cambridge, Massachusetts**	**02141**
(Address of principal executive offices)	**(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 every Interactive Data File required to be submitted 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 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	☐	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, 2018, 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 $1,631,271,034.00 based upon the closing price of the registrant's Common Stock on June 29, 2018, the last business day of the registrant's most recently completed second fiscal quarter.

The number of shares of the registrant's Common Stock outstanding as of February 8, 2019 was 49,092,251.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2019 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, 2018 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, clinical stage genome editing company dedicated to developing potentially transformative genomic medicines 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 genome editing into a broad class of transformative genomic medicines to benefit the greatest number of patients.

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, also known as Cas12a), 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. 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 diseases.

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 over 95% of the human genome. Each of our product candidates derives from our platform, and we plan to continue to use our platform to develop a broad range of genomic medicines to treat serious diseases.

Our product development strategy is to target genetically addressable diseases where gene editing can be used to enable or enhance therapeutic outcomes for patients. Genetically addressable diseases include genetically defined diseases that may be treated by correcting a disease-causing gene and genetically treatable diseases that do not necessarily have a single, disease causing gene, but which nonetheless may be treated by editing the genome to ameliorate or eliminate the signs or symptoms of the disease. We are advancing both *in vivo* CRISPR medicines, in which the medicine is injected or infused into the patient to edit the cells inside their body, and engineered cell medicines, in which cells are edited with our technology and then administered to the patient. While our discovery efforts have ranged across several different genetically addressable diseases and therapeutic areas, the two areas where our programs are more mature are ocular diseases and engineered cell medicines to treat blood diseases and cancer.

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 other potential treatment in clinical trials in the United States and Europe. A mutation in the CEP290 gene causes LCA10. 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*. In October 2018, we filed an investigational new drug application (“IND”) for a Phase 1/2 clinical trial for EDIT-101 for treatment of LCA10, which was accepted by the United States Food and Drug Administration (the “FDA”) in November 2018. We and our partner Allergan Pharmaceuticals International Limited (“Allergan”) plan to initiate patient screening in mid-2019 and begin patient dosing in the second half of 2019, enrolling approximately 10 to 20 patients in the United States and Europe. In addition, we initiated a clinical natural history study in 2017 to evaluate the clinical course and characteristics of LCA10 more extensively. We believe preclinical results to date with EDIT-101 validate our platform technology, including its potential application to other ocular diseases, such as Usher syndrome 2A (“USH2A”), retinitis pigmentosa and recurrent ocular herpes simplex virus 1 (“HSV-1”), as well as diseases of other organs and tissues.

In March 2017, we entered into a strategic alliance and option agreement with 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 EDIT-101, and will be responsible for development and commercialization of any program with respect to which it exercises its option. We received an upfront payment of $90.0 million from Allergan and have the potential to receive greater than $1.0 billion in contingent milestone payments, as well as high single-digit royalties on programs for which Allergan exercises its option. Under our alliance with Allergan, we had the right to elect to co-develop and share equally in the profits and losses in the United States for up to two programs for which Allergan exercise its option, including the LCA10 program. In August 2018, Allergan exercised its option for the LCA10 program and paid us $15.0 million in connection with such exercise and we subsequently entered into a co-development and commercialization agreement with an affiliate of Allergan under which we will equally split profits and losses for EDIT-101 in the United States with Allergan (the "LCA10 Co-Development and Commercialization Agreement"). We also retain the option to co-develop and commercialize one additional program in the United States pursuant to our alliance with Allergan. We also received a $25.0 million payment from Allergan in connection with the acceptance of the IND for EDIT-101.

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 developed. To this end, we have established 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 blood diseases and cancer. More broadly, we believe that our editing capabilities can be applied to many additional cell types, including natural killer cells.

In May 2015, we established a collaboration with Juno Therapeutics, Inc., a Celgene company that is a wholly-owned subsidiary of Celgene Corporation ("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, four milestone payments totaling $10.0 million related to technical progress in research programs under the collaboration and a $5.0 million payment in connection with amending the collaboration agreement in May 2018. We also have the potential to receive approximately $920 million in aggregate 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, of which we have received $9.5 million as of December 31, 2018.

We are also developing a novel gene editing approach to treating sickle cell disease and beta-thalassemia, together referred to as hemoglobinopathies. This program takes advantage of our genome editing capabilities in hematopoietic stem cells ("HSCs"), including a distinct genome editing approach that targets the hemoglobin gene locus directly. We believe this has the potential to effectively and durably treat hemoglobinopathies and may have advantages over other programs which increase fetal hemoglobin indirectly by altering the expression of other genes.

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 as we are pioneering the possible.

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 ("DMD"), 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.

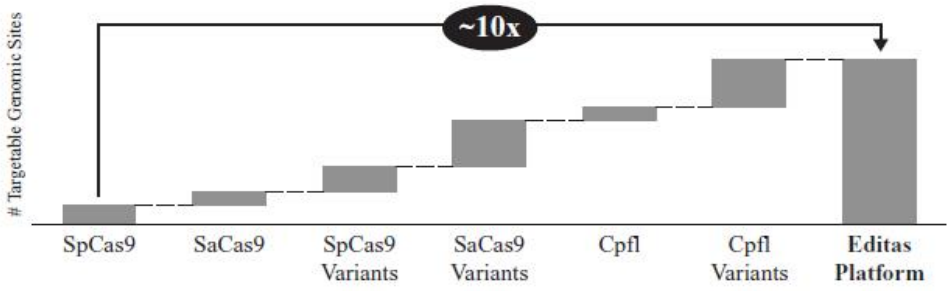
Nuclease and Guide RNA Engineering

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, 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 90% *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.

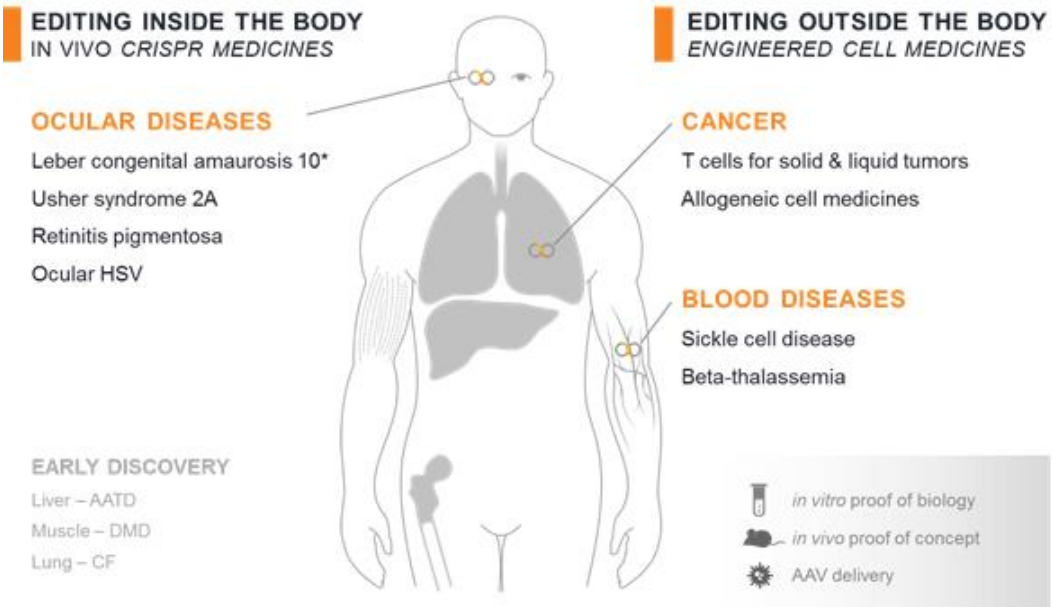
Directed Editing

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 product development strategy is to target genetically addressable diseases where gene editing can be used to enable or enhance therapeutic outcomes for patients. While our discovery efforts have ranged across several different genetically addressable diseases and therapeutic areas, the two areas where our programs are more mature are ocular diseases and engineered cell medicines to treat blood diseases and cancer. 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 genetically addressable 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 EDIT-101. As discussed above, Allergan has exercised its option with respect to EDIT-101 and entered into a profit-sharing arrangement with us in the United States for such 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 cells and function 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 a disease-causing 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 improve vision or arrest the further loss of vision in LCA patients.

In 2017, we initiated a natural history study of LCA10 patients. In this study, we intend to assess the manifestations and course of the LCA10 disease in approximately 40 patients across a range of ages and disease severity at seven sites in the United States and Europe. Patients will be evaluated six times over the course of a year. The purpose of the study is to inform the clinical trial design and enrollment for our Phase 1/2 clinical trial of EDIT-101 through the characterization of patients' baseline status and the rate of change of the disease, as well as to validate endpoints of the Phase 1/2 clinical trial for EDIT-101.

In October 2018, we filed an IND for a Phase 1/2 clinical trial for EDIT-101, which was accepted by the FDA in November 2018. We and Allergan designed an initial Phase 1/2 clinical trial which is an open-label, single ascending dose trial of EDIT-101 in adult and pediatric (i.e., ages 3 to 17 years) patients with retinal degeneration caused by a homozygous or compound heterozygous mutation of the CEP290 gene, which is referred to as an IVS26 mutation. Patients will receive a single dose of EDIT-101 administered via subretinal injection in one eye. Approximately 10 to 20 patients will be enrolled at approximately eight trial centers in the United States and Europe. Up to five cohorts across three doses will be enrolled in this clinical trial. The primary endpoint of the trial is an assessment of safety and tolerability, and the secondary endpoint is to evaluate the efficacy of a single dose of EDIT-101 on change from baseline in various parameters. Efficacy will be evaluated at multiple timepoints, including core measures every three months for the first year and then less frequently thereafter. We and Allergan plan to initiate patient screening in mid-2019 and begin patient dosing in the second half of 2019.

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 vision 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 non-human 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. Furthermore, these doses were shown in subsequent studies to be well tolerated in non-human primates based on visual and immunohistochemical analysis. Similar studies in mice showed that editing was rapid, achieving maximum levels by 6 weeks, and stable with changes maintained for the 26 weeks of the study.

In addition, we developed a retinal explant system to explore the potential effectiveness of 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 USH2A, retinitis pigmentosa and HSV-1. 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 and testing of the components of the AAV vector we are pursuing for EDIT-101 will continue to inform our approach to treating the most common cause of USH2A.

Usher Syndrome 2A

USH2A gene mutations are the most common cause of Usher syndrome, a form of RP 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. In preclinical studies, we have shown that both wild-type usherin and usherin-lacking amino acids encoded by exon 13 restore cilia formation to cells lacking usherin. In our research program, we aim to develop a therapeutic that will skip exon 13 which contains the mutation.

Retinitis Pigmentosa

Mutations in the human rhodopsin (“RHO”) gene accounts for 25% of all autosomal dominant forms of retinitis pigmentosa (“adRP”), a progressive form of retinal degeneration characterized by initial night blindness early in life followed by loss of peripheral vison and eventual complete blindness. More than 150 mutations in the RHO gene have been identified, with the most prevalent allele in the United States representing approximately 10 percent of all patients with adRP. We are investigating a novel approach to address all forms of adRP resulting from mutations in the RHO gene.

Herpes Simplex Virus 1

HSV-1 causes lifelong infections leading to ocular and oral disease. Infected individuals develop persistent latent infections in the nerves that innervate 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 HSV-1 DNA with the goal of eliminating or reducing reactivation.

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, 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 have optimized genome editing components and delivery methods compatible with engineered T cell manufacturing methods developed by Juno Therapeutics.

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 adverse, functionality. We believe this innovation may broaden the therapeutic opportunity for engineered T cells.

Non-malignant Hematologic Diseases

We are developing an approach for genome editing in HSCs to support the advancement of research programs to treat non-malignant hematological diseases, such as sickle cell disease and beta thalassemia. We are actively pursuing a distinct gene editing approach to treating these hemoglobinopathies and assessing other opportunities to develop medicines for diseases where we believe gene editing of HSCs is likely to produce a therapeutic effect.

Our genome editing approach in HSCs focuses on the hemoglobin locus with the aim of developing best-in-class medicines for sickle cell disease and beta thalassemia. Our primary criteria for a successful product candidate are successful editing in HSCs, maintenance of normal HSC function, and a durable predicted therapeutic induction of fetal hemoglobin. We have focused these efforts on directly editing a 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. Using this approach in preclinical studies, we edited human CD34+ cells at the *HBG1/2* promoter site and then infused these edited cells into immuno-compromised mice. Following such infusion, we collected bone marrow from the mice at eight- and 16-weeks post-infusion. Such studies demonstrated that the edited cells were able to repopulate all hematopoietic lineages, including red blood cell precursors, in the mice, resulting in increased production of fetal hemoglobin. In contrast, we found that cells edited at the *BCL11A* erythroid enhancer site were not able to repopulate the erythroid lineage in mice. If these results are seen in humans, then editing at such site may not be an effective approach to treat sickle cell disease or beta-thalassemia. For this reason, we believe our approach of editing the hemoglobin locus to increase fetal hemoglobin has the potential to generate differentiated medicines to benefit patients with sickle cell disease and beta thalassemia.

Early Discovery Programs

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 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. We continue to evaluate whether to pursue developing a treatment to potentially treat patients with DMD.

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 continue to evaluate whether to pursue developing a treatment to potentially treat patients with CF.

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 and we continue to evaluate whether to pursue developing a treatment using this approach to treat patients with A1AT.

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. We and Juno Therapeutics amended and restated this agreement in May 2018. Under this agreement, Juno Therapeutics and we will research and develop CAR and TCR engineered T cell products across four research programs over a five-year period, ending in May 2020. Juno Therapeutics has the option to extend the research period through May 2022, upon us agreeing to extend the term and the 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 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. We also granted Juno Therapeutics a non-exclusive, worldwide, non-sublicensable license to certain of our patent applications related to our proprietary genome editing detection method for Juno Therapeutics' internal research purposes. 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 subject to certain exceptions, 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 agreement and except pursuant to the 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 agreement and except pursuant to the 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 four 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 agreement, we received an upfront payment of $25.0 million, an amendment fee of $5.0 million and we have received four milestone payments totaling $10.0 million under the collaboration for technical progress in three 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 four programs under our collaboration, subject to adjustment in accordance with the terms of the agreement, of which we had recognized $17.7 million as of December 31, 2018. 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 four research programs, of which we have achieved four 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 four 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 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 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.

Allergan Strategic Alliance and Option Agreement and Co-Development and Commercialization 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 EDIT-101, for which Allergan has exercised its option. 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. Allergan has also paid us $15.0 million in connection with Allergan exercising its option for the LCA10 program and $25.0 million in connection with the acceptance of the IND for 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.

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.

We have the right to elect to participate in a profit-sharing arrangement with Allergan in the United States for one additional Collaboration Development Program that Allergan exercises its option with respect to, on terms mutually agreed by us and Allergan and subject to a right of Allergan to reject such election under certain circumstances. If we make such an election, 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 (i) 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 (ii) 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.

In February 2019, we entered into the LCA10 Co-Development and Commercialization Agreement with Allergan Sales, LLC ("Allergan Sales"). Under this agreement, we and Allergan Sales have agreed to share in the costs and certain development responsibilities for products arising under the program to treat LCA10 and the profits and losses resulting from the commercialization of any products arising under such program, in each case, in the United States.

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 -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 compositions of matter and their use for genome editing and to certain CRISPR/Cas9 related delivery technologies. Pursuant to the Cas9-I License Agreement, and as of December 31, 2018, we have certain rights under 43 U.S. patents, 61 pending U.S. patent applications, 14 European patents and related validations, 39 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 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 has been conformed 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 "Risk Factors—Risks Related to Our Intellectual Property—Some of Our In-Licensed Patents are Subject to Priority and Validity Disputes" in Part I, Item 1A 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, had the right to receive a low to mid double-digit percentage of the sublicense income, which percentage decreased to a low double-digit percentage in 2018 and may still decrease to a low of a high single-digit percentage for licensed products for the prevention or treatment of human disease under sublicenses executed after we meet a certain clinical milestone.

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. 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, 2018, we have certain rights under one U.S. patent, nine pending U.S. patent applications, one European patent and related validations, seven pending European 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 Cpf1Third 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, which we settled in full in 2017. 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”). Market Cap Success Payments are payable by us in cash or in the form of promissory notes (the “Promissory Notes”).The Promissory Notes bear interest at 4.8% per annum. Principal and interest on the Promissory Notes are payable on, subject to certain exceptions, 150 days following issuance (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 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 are required to pay all remaining principal and accrued interest on the Promissory Notes in cash within a specified period following such event. 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 2017, two Market Cap Success Payments of $5.0 million each became due and payable and we issued Promissory Notes in such amounts, which we fully settled by issuing shares of our common stock in 2017 and 2018. The remaining Success Payments that may be paid to Broad and Wageningen range from a low-eight digit dollar amount to a mid-eight digit dollar amount, and collectively will not exceed, in aggregate, $115.0 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.

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, 2018, we have certain rights under 13 pending U.S. patent applications, one European patent and related validations, 12 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, which was settled in January 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.

Broad Sponsored Research Agreement

In June 2018, we entered into a sponsored research agreement (the "Sponsored Research Agreement") with Broad providing for Broad to conduct research useful or relevant to genome editing in the field of genomic medicines for the prevention or treatment of human disease with funding from us. Under the Sponsored Research Agreement, Broad granted us an exclusive right of first negotiation for licenses from Broad with respect to patentable inventions developed by Broad in the course of the sponsored research, subject to certain limitations and retained rights ("Sponsored Invention Licenses").

Under the Sponsored Research Agreement, we are obligated to make payments of research funding to Broad in the event our market capitalization reaches specified thresholds ranging from a mid nine digit dollar amount to a low eleven digit dollar amount ("Market Cap Research Funding") or a sale of our company for consideration ranging from a mid nine digit dollar amount to a low eleven digit dollar amount ("Company Sale Research Funding" and, collectively with the Market Cap Research Funding, the "Research Funding"). In connection with entering into the Sponsored Research Agreement, we stipulated that the first two research payments of $5 million and $7.5 million were due and payable to Broad (the "Initial Research Payments"). Other than the Initial Research Payments, we are not required to make additional Research Funding payments if we, whether directly or through our affiliates or sublicensees, are not researching, developing, or commercializing products based on or incorporating inventions exclusively licensed to us

from Broad under the Sponsored Invention Licenses or based on or incorporating CRISPR technology owned, co-owned, or controlled by Broad and otherwise licensed to us, subject to certain exclusions (an "Applicable Product" and such exemption from payment, the "Funding Exemption"). In the event that we, whether directly or through our affiliates or sublicensees, later resume research, development, or commercialization of an Applicable Product within a specified period of time, any Research Funding that was not paid to Broad as a result of the Funding Exemption shall become payable. Under the Sponsored Research Agreement, we are obligated to pay up to a maximum of $125 million to Broad in Research Funding, inclusive of the Initial Research Payments, and in no event shall the aggregate amount of all Research Funding exceed such amount.

Company Sale Research Funding is payable solely in cash. Unless we have undergone a change in control, Market Cap Research Funding is payable by us in cash or in the form of promissory notes bearing interest at a rate of 4.8% per year. Principal and interest on such notes will be payable over a term running through the 150 days following issuance, provided that full payment of any such notes is due within a specified period of time following a sale or change of control event with respect to our company. Under the terms of the notes, the entire unpaid principal and interest of the notes shall become immediately due and payable upon a payment default or bankruptcy- and insolvency-related defaults. At our option, the notes are payable in cash or convertible into our common stock of subject to certain conditions. Following a change in control of our company, Market Cap Research Funding is required to be made in cash. In connection with the Initial Research Payment, we issued promissory notes to Broad in the aggregate principal amount of $12.5 million (the "Initial Notes"), of which $5.0 million is due and payable in November 2018 and $7.5 million is due in April 2019. Interest does not commence accruing on $7.5 million of the principal until November 2018. In June 2018, we settled the outstanding principal and accrued interest on these notes by issuing shares of our common stock to Broad.

The Sponsored Research Agreement is terminable by each party upon the occurrence of specified bankruptcy events of the other party and otherwise will continue in effect until the later of the expenditure of all Research Funding by Broad and such time as we have no further rights of first negotiation for Sponsored Invention Licenses, unless otherwise mutually agreed between the parties.

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."

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, 2018, we owned four U.S. patents, 34 pending U.S. non-provisional patent applications, two European patents and related validations, 29 pending European patent applications, nine pending U.S. provisional patent applications, 19 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, one of these European patents and their U.S., European 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, four of these pending PCT patent applications, one of these pending U.S. non-provisional patent applications and one of these pending U.S. provisional patent applications are co-owned with certain of our collaborators because they encompass inventions developed under our collaborations. Our current issued U.S. patents, if the appropriate maintenance fees are paid, are expected to expire between 2034 and 2037, excluding any additional term for patent term adjustments or patent term extensions. 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 2039, excluding any additional term for patent term adjustments or patent term extensions.

As of December 31, 2018, we in-licensed 50 U.S. patents, 16 European patents and related validations, and over 550 pending patent applications, including approximately 92 pending U.S. non-provisional patent applications, 64 pending European patent applications, and other related patents and patent applications in jurisdictions outside the United States and Europe that are related to our CRISPR technology collectively from various universities and institutions. 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. 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. 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 2033 and 2036, excluding any additional term for patent term adjustments or patent term extensions.

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."

LCA10

As of December 31, 2018, we owned one U.S. patent, three pending U.S. non-provisional patent applications, one pending European patent application, one pending Canadian patent application, one pending U.S. provisional 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. Our current issued U.S. patent, if the appropriate maintenance fees are paid, is expected to expire in 2035, excluding any additional term for patent term extensions. 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 2039, excluding any additional term for patent term adjustments or patent term extensions.

Trademarks

As of December 31, 2018, 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, China, the European Union, Japan 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, genome editing and cell therapy 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 or therapies using CRISPR technology include Arbor Biotechnologies, Caribou Biosciences, Casebia Therapeutics, CRISPR Therapeutics, ERS Genomics, Exonics Therapeutics, Intellia Therapeutics, Locus Biosciences, ToolGen Inc. 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 base editing, transcription activator-like effector nucleases, meganucleases, Mega-TALs and zinc finger nucleases. The companies developing these other genome editing technologies include Beam Therapeutics Inc., 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, Sarepta Therapeutics, Solid Biosciences, Spark Therapeutics, uniQure and Voyager Therapeutics. In addition to competition from other genome editing therapies, gene therapies or cell medicine therapies, any products that we may develop may

also face competition from other types of therapies, such as small molecule, antibody, protein, oligonucleotide, or ribonucleic acid therapies. For example, ProQR Therapeutics N.V. is conducting a Phase I/II clinical trial for its experimental treatment using antisense oligonucleotide technology for LCA10.

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 have limited manufacturing operations and do not own or operate any substantial 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. Additionally, under the LCA10 Co-Development and Commercialization Agreement, Allergan will be responsible for all commercialization efforts with respect to EDIT-101.

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, reimbursement, sales, 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. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or chemistry, manufacturing, and controls. 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.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called “compassionate use,” is the use of investigational products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational products for patients who may benefit from investigational therapies. FDA regulations allow access to investigational products under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the investigational product under a treatment protocol or treatment IND application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

On December 13, 2016, the 21st Century Cures Act established (and the 2017 Food and Drug Administration Reauthorization Act later amended) a requirement that sponsors of one or more investigational products for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. Although these requirements were rolled out over time, they have now come into full effect. This provision requires drug and biologic companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the investigational drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a manufacturer to make its investigational products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

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.

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.

Information about clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its ClinicalTrials.gov website. Similar requirements for posting clinical trial information are present in the European Union (EudraCT) website: https://eudract.ema.europa.eu/ and other countries, as well.

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, including draft guidance documents released in July 2018 relating to gene therapies for human retinal disorders and gene therapies for rare diseases. 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 2019 is $2,588,478 for an application requiring clinical data. The sponsor of an approved BLA is also subject to an annual program fee, which for fiscal year 2019 is $309,915. 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 Exclusivity

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, 2019, the FDA has approved 17 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 2019, the standard fee for review of a PMA is $322,147 and the small business fee is $80,537.

A clinical trial is typically required for a PMA application and, in a small percentage of cases, the FDA may require a clinical study in support of a 510(k) submission. A manufacturer that wishes to conduct a clinical study involving the device is subject to the FDA's IDE regulation. The IDE regulation distinguishes between significant and non-significant risk device studies and the procedures for obtaining approval to begin the study differ accordingly. Also, some types of studies are exempt from the IDE regulations. A significant risk device presents a potential for serious risk to the health, safety, or welfare of a subject. Significant risk devices are devices that are substantially important in diagnosing, curing, mitigating, or treating disease or in preventing impairment to human health. Studies of devices that pose a significant risk require both FDA and an IRB approval prior to initiation of a clinical study. Non-significant risk devices are devices that do not pose a significant risk to the human subjects. A non-significant risk device study requires only IRB approval prior to initiation of a clinical study.

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.

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 is expected to become applicable later in 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.

The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. If no formal withdrawal agreement is reached between the United Kingdom and the European Union, then it is expected the United Kingdom's membership of the European Union will automatically terminate two years after the submission of the notification of the United Kingdom's intention to withdraw from the European Union. Discussions between the United Kingdom and the European Union focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on March 29, 2019 without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation ("GDPR"), which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

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 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 health care benefits, items or services;

- the Foreign Corrupt Practices Act, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;

- 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.

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. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". The Congress will likely consider other legislation to replace elements of the ACA during the next Congressional session. 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 ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state 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. For example, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state 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. For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services will take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases.

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

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, 2018, 2017 and 2016.

Employees

As of February 1, 2019, we had 133 full-time employees, including 41 employees with M.D. or Ph.D. degrees. Of these full-time employees, 81 employees are engaged in research and development activities. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Our Corporate Information

We were incorporated under the name Gengine, Inc. 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 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 (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 $110.0 million, $120.3 million, $97.2 million, and $72.9 million for the years ended December 31, 2018, 2017, 2016 and 2015, respectively. As of December 31, 2018, we had an accumulated deficit of $416.3 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., a Celgene company that is a wholly-owned subsidiary of Celgene Corporation ("Juno Therapeutics"), and payments under our strategic alliance with Allergan Pharmaceuticals International Limited ("Allergan"). We have devoted substantially 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;
- prepare for and initiate clinical development of EDIT-101 to treat Leber congenital amaurosis ("LCA") 10 ("LCA10");
- 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 only recently begun preparing for the initiation of clinical development of EDIT-101 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. Other than EDIT-101, 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. 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, 2018 and anticipated interest income 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 for and initiating the clinical development of EDIT-101 to treat LCA10;
- 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 additional 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, 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, undertaking preclinical studies and preparing to undertake clinical trials. Except for EDIT-101 to treat LCA10, all of our research programs are still in the preclinical or research stage of development, and their risk of failure of all of our research programs is high. We have not yet demonstrated an ability to successfully initiate or 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 collaboration 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;
- 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. Because we have not initiated a clinical trial for any program and most of 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. 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 understanding and 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, academic scientists in several countries, including the United States, have reported on their attempts to edit the genome of human embryos as part of basic research. In addition, in November 2018, it was reported that Dr. Jiankui He, a Chinese biophysics researcher who was an associate professor in the Department of Biology of the Southern University of Science and Technology in Shenzhen, China, claimed he had created the first human genetically edited babies, twin girls. This claim, and another that Dr. He had helped create a second gene-edited pregnancy, was subsequently confirmed by Chinese authorities and was negatively received by the public, in particular those in the scientific community. In the United States, germline editing for clinical application has been expressly prohibited since enactment of a December 2015 U.S. Food and Drug Administration ban on such activity. Prohibitions are also in place in the United Kingdom, across most of Europe, in China, and many other countries around the world. In the United States, 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. 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. Basic research on embryos is more tightly controlled in many other European countries.

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. Other than EDIT-101 to treat LCA10, all of our product development

programs are still in the preclinical or research stage of development. Our research programs, including those subject to our collaboration with Juno Therapeutics and our 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 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 certain 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 EDIT-101. Except for EDIT-101, 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 and development of EDIT-101 to treat 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 EDIT-101 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 clinical trials for EDIT-101;
- 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.

The foregoing also applies to our collaborators to the extent we have partnered, sold or licensed any of our research programs to them. For instance, Allergan has exercised its option to license EDIT-101 and, although we have entered into a profit-sharing arrangement to equally split the profits and costs of such program in the United States and we will continue to work with Allergan on the development and commercialization of such program, in the event a dispute arises, Allergan will have final decision making authority. If we or our collaborators 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 or our collaborators will successfully develop or commercialize EDIT-101, or any of our other research programs. If we or any of our collaborators and 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 history, if any, 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 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 history, if any, 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 ("IECs") 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 patients 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 IECs 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 patients 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 challenging for the rare genetically defined diseases we are targeting. 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. For example, ProQR Therapeutics N.V. has already enrolled LCA10 patients in its clinical trial, which may limit the number of potential patients available to enroll in the planned Phase 1/2 clinical study for EDIT-101.

Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- size of the patient population and process for identifying patients;
- 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 patient informed consent;
- risk that enrolled patients 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, EDIT-101 for the treatment of LCA10 has 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 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, genome editing and cell therapy 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. Other companies developing CRISPR technology or therapies using CRISPR technology include Arbor Biotechnologies, Caribou Biosciences, Casebia Therapeutics, CRISPR Therapeutics, ERS Genomics, Exonics Therapeutics, Intellia Therapeutics, Locus Biosciences, ToolGen Inc. (“ToolGen”) 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 base editing, transcription activator-like effector nucleases, meganucleases, Mega-TALs, and zinc finger nucleases. These companies include Beam Therapeutics Inc., 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, Sarepta Therapeutics, Solid Biosciences, Spark Therapeutics, uniQure and Voyager Therapeutics. In addition to competition from other genome editing therapies, gene therapies or cell medicine therapies, any products that we may develop may also face competition from other types of therapies, such as small molecule, antibody, protein, oligonucleotide, or ribonucleic acid therapies. For example, ProQR Therapeutics N.V. is conducting a Phase I/II clinical trial for its experimental treatment using antisense oligonucleotide technology for LCA10.

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.

Some of our most advanced programs, including EDIT-101, focus 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, including the planned Phase 1/2 clinical trial for EDIT-

101, 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 ensure sufficient clinical material for any clinical trials we may be conducting or are planning to conduct and meet market demand for any products we develop and commercialize. For example, if the contract manufacturing organizations that we have engaged to manufacture EDIT-101 fail to deliver sufficient amounts or fail to timely deliver EDIT-101 due to any of the risks discussed herein, then we and Allergan may not be able to begin patient dosing in the planned Phase 1/2 clinical trial for EDIT-101 in the second half of 2019.

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 any additional options 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 have a limited ability to manufacture materials for our research programs and preclinical studies and we do not operate any significant manufacturing facilities. We primarily 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 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 $14.2 million, $18.7 million, $23.6 million, and $9.4 million during the years ended December 31, 2018, 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.

On April 12, 2017, the University of California, the University of Vienna, and Emmanuelle Charpentier appealed to the U.S. Court of Appeals for the Federal Circuit for review of the no interference-in-fact holding made by the PTAB in the interference proceeding. On September 10, 2018, the Court of Appeals for the Federal Circuit (the "CAFC") affirmed the PTAB's holding of no interference-in-fact. The University of California, the University of Vienna, and Emmanuelle Charpentier did not appeal to the U.S. Supreme Court for review of this decision. The judgment of no interference-in-fact is therefore final and 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 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. For example, 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. On January 3, 2019, the PTAB lifted the suspension in light of the CAFC's affirmance 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.

In addition, a petition for post-grant review was filed by Benson Hill Biosystems, Inc. ("Benson Hill") with the PTAB on July 17, 2018 against one patent that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard (U.S. Patent No. 9,790,490). This patent relates generally to the CRISPR/Cpf1 system and its use in eukaryotic cells. Post-grant review is a procedure through which a third party can request the PTAB to review the patentability of one or more claims of a granted patent on any ground that could be raised in an invalidity defense. The post-grant review process begins with a third party filing a petition on or prior to the date that is nine months after the grant of the patent. The patent owner may file a preliminary response to the petition. A post-grant review may then be instituted by the PTAB but only upon a showing that, it is more likely than not that at least one claim challenged is unpatentable. If the proceeding is instituted and not dismissed, a final determination by the PTAB will be issued within one year (extendable for good cause by six months). Broad, acting on behalf of itself, MIT and Harvard, filed a preliminary response to the petition on October 24, 2018. On January 22, 2019, the PTAB notified the parties that it would not be instituting post-grant review of U.S. Patent No. 9,790,490 based on Benson Hill's petition.

We or our licensors may also 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. On February 18, 2019, one additional European patent (European Patent No. EP 2,784,162 B1) that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard was revoked in its

entirety and another European patent (European Patent No. EP 2,896,697 B1) that we in-license from such parties was maintained with amended patent claims. The Opposition Division has also initiated opposition proceedings against seven other European patents that we have in-licensed from Broad, acting on behalf of itself, MIT and Harvard (European Patent Nos. EP 2,898,075 B1, EP 2,921,557 B1, EP 2,931,897 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), 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), and one European patent that we co-own and in-license from Broad, acting on behalf of itself, MIT and The University of Iowa Research Foundation (European Patent No. EP 3,066,201 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. The loss of priority for, or the loss of, these European patents could have a material adverse effect on the conduct of our business. One or more of the third parties that have filed oppositions against these European patents or other third parties may file future oppositions against other European patents that we in-license or own.

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 several of our in-licensed European patents and additional interference, re-examination, post-grant review, *inter partes* review, opposition, and other intellectual property proceedings may be initiated in the future. The opposition proceedings have so far resulted in the revocation of two of our in-licensed European patents while maintaining a third European patent with amended claims. 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 No. 10,000,772 and 10,113,167 and other related U.S. patent applications and foreign counterparts including European Patent Nos. EP 2,800,811 B1 and EP 3,241,902 B1 which are 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 including European Patent No. EP 2,912,175 B1 which is being opposed by several parties) filed by ToolGen, and WO 2014/089290 (and its related U.S. patent applications and foreign counterparts including European Patent Nos. EP 3,138,910 B1, EP 3,138,911 B1, and EP 3,138,912 B1 which are being opposed by several parties) filed by Sigma-Aldrich Co. LLC. 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 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.

The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. If no formal withdrawal agreement is reached between the United Kingdom and the European Union, then it is expected the United Kingdom's membership of the European Union will automatically terminate two years after the submission of the notification of the United Kingdom's intention to withdraw from the European Union. Discussions between the United Kingdom and the European Union focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on March 29, 2019 without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

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.

Since enactment of the ACA, 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. Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session. It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provision.

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.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

The costs of prescription pharmaceuticals 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 and enacted 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, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, 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, legislatures are increasingly 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.

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

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 attract and retain key executives and to attract, retain, and motivate qualified personnel.

We are highly dependent on the principal members of our management and scientific teams. Each of these individuals is employed "at will," meaning we or the individual 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. Additionally, although we have an interim Chief Executive Officer and will have an interim Chief Financial Officer following the impending departure of our Chief Financial Officer, we are actively trying to recruit candidates to fill these positions, as well as a Chief Medical Officer, permanently and any inability to fill these position in an expedient manner may have a material adverse effect on our business.

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, including a permanent Chief Executive Officer and Chief Financial Officer and a Chief Medical Officer, 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, clinical, manufacturing 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 132 as of December 31, 2018. 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 may 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, including our financial systems. 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 clinical trials for EDIT-101 and any preclinical studies and clinical trials of any other 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, including our Chief Executive Officer, Chief Financial Officer and Chief Medical Officer, or departure of key personnel, including the recent departures of our former Chief Executive Officer and former Chief Medical Officer, and the impending departure of our Chief Financial Officer;
- 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. 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 participant establishing the plan when entering into the plan, without further direction from such participant. 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.

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 we have incurred, and will continue to 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 and are required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To maintain compliance with SOX Section 404, we will continue to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to dedicate internal resources, 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. 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. Certain of our intellectual property rights, including ones licensed to us under our licensing agreements, are subject to, and from time to time may be subject to, priority and validity disputes. For additional information regarding these matters, see “Item 1A. Risk Factors—Risks Related to Our 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.

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.

Holders

As of February 15, 2019, we had approximately 19 holders of record of our common stock. This number does not include beneficial owners whose shares were held in street name.

Dividend Policy

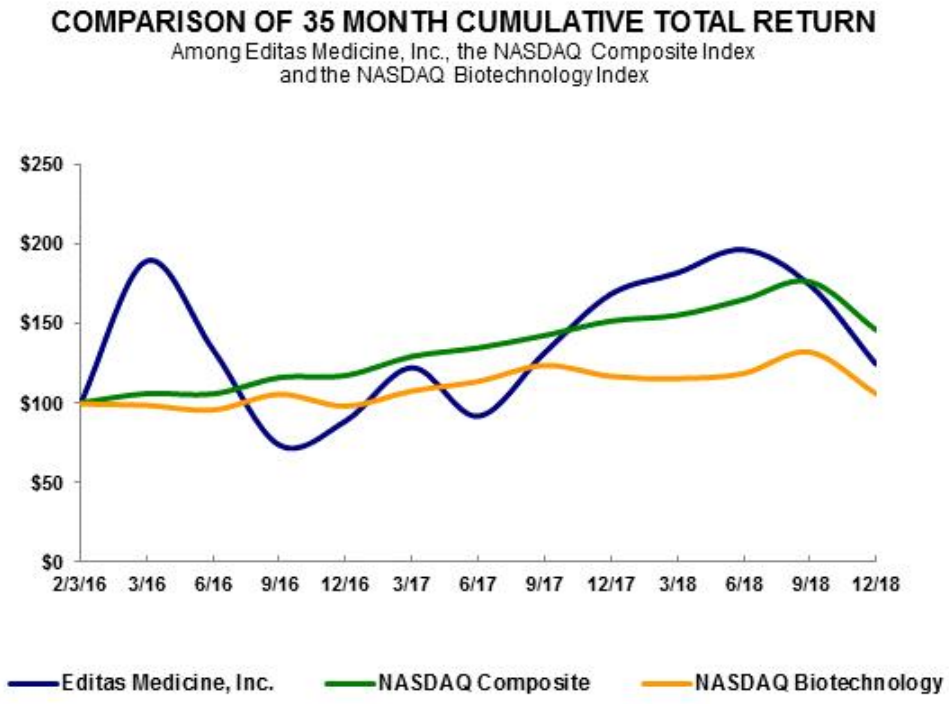
We have never declared or paid any cash dividends on our common stock. We currently intend to retain future earnings to fund the development and growth of our business. We do not expect to pay any cash dividends in the foreseeable future. In addition, the terms of any future debt agreements that we may 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, 2018. 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

None.

Purchases of Equity Securities by the Issuer and Affiliates Purchasers

Neither we nor any affiliated purchaser or anyone acting on behalf of us or an affiliated purchaser made any purchases of shares of our common stock during the fourth quarter of 2018.

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, 2018, 2017 and 2016 and the consolidated balance sheet data as of December 31, 2018 and 2017 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 years ended December 31, 2015 and 2014 and consolidated balance sheet data as of December 31, 2016, 2015 and 2014 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. Our consolidated statements of operations are summarized as follows (in thousands, except share and per share amounts):

	Year Ended December 31,				
	2018	2017	2016	2015	2014
Consolidated Statements of Operations Data:					
Collaboration and other research and development revenues	$ 31,937	$ 13,728	$ 6,053	$ 1,629	$ —
Operating expenses:					
Research and development	90,654	83,159	56,979	18,846	5,073
General and administrative	55,010	50,502	46,262	18,095	7,650
Total operating expenses	145,664	133,661	103,241	36,941	12,723
Operating loss	(113,727)	(119,933)	(97,188)	(35,312)	(12,723)
Other income (expense), net	328	587	(57)	(37,445)	(928)
Interest income (expense), net	3,445	(978)	62	(143)	(34)
Total other income (expense), net	3,773	(391)	5	(37,588)	(962)
Net loss	$ (109,954)	$ (120,324)	$ (97,183)	$ (72,900)	$ (13,685)
Reconciliation of net loss to net loss attributable to common stockholders:					
Net loss	$ (109,954)	$ (120,324)	$ (97,183)	$ (72,900)	$ (13,685)
Accretion of redeemable convertible preferred stock to redemption value [1]	—	—	(47)	(394)	(309)
Net loss attributable to common stockholders [1]	$ (109,954)	$ (120,324)	$ (97,230)	$ (73,294)	$ (13,994)
Net loss per share attributable to common stockholders, basic and diluted [1]	$ (2.33)	$ (2.98)	$ (3.02)	$ (28.55)	$ (12.46)
Weighted-average common shares outstanding, basic and diluted [1]	47,097,735	40,323,631	32,219,717	2,566,916	1,123,098

(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,				
	2018	2017	2016	2015	2014
Consolidated Balance Sheet Data:					
Cash, cash equivalents, and marketable securities	$ 368,955	$ 329,139	$ 185,323	$ 143,180	$ 10,623
Working capital	338,876	295,492	154,100	138,060	4,555
Total assets	420,386	373,260	229,182	149,363	12,188
Deferred revenue, net of current portion	115,614	94,725	26,000	25,321	—
Construction financing lease obligation, net of current portion	32,417	33,431	35,096	—	—
Equipment loan, net of current portion and discounts	—	—	—	—	344
Redeemable convertible preferred stock	—	—	—	199,915	20,772
Total stockholders' equity (deficit)	236,162	208,080	134,607	(83,114)	(15,292)

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, clinical stage genome editing company dedicated to developing potentially transformative genomic medicines to treat a broad range of serious diseases. We have developed a proprietary genome editing platform based on CRISPR technology and we continue to expand its capabilities. Our product development strategy is to target genetically addressable diseases where gene editing can be used to enable or enhance therapeutic outcomes for patients. Genetically addressable diseases include genetically defined diseases that may be treated by correcting a disease-causing gene and genetically treatable diseases that do not necessarily have a single, disease causing gene, but which nonetheless may be treated by editing the genome to ameliorate or eliminate the signs or symptoms of the disease. We are advancing both *in vivo* CRISPR medicines, in which the medicine is injected or infused into the patient to edit the cells inside their body, and engineered cell medicines, in which cells are edited with our technology and then administered to the patient. While our discovery efforts have ranged across several different genetically addressable diseases and therapeutic areas, the two areas where our programs are more mature are ocular diseases and engineered cell medicines to treat blood diseases and cancer.

In ocular diseases, our most advanced program is designed to address a specific genetic form of retinal degeneration called Leber congenital amaurosis 10 ("LCA10"), a disease for which we are not aware of any available therapies and only one other potential treatment in clinical trials in the United States and Europe. In October 2018, we filed an investigational new drug ("IND") application for a Phase 1/2 clinical trial for EDIT-101, our experimental medicine to treat LCA10, which was accepted by the United States Food and Drug Administration ("FDA") in November 2018. We and our partner Allergan Pharmaceuticals International Limited ("Allergan") plan to initiate patient screening in mid-2019 and begin patient dosing in the second half of 2019, enrolling approximately 10 to 20 patients in the United States and Europe.

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.

In May 2015, we entered into a collaboration with Juno Therapeutics, Inc., a Celgene company that is a wholly-owned subsidiary of Celgene Corporation ("Juno Therapeutics"), a leader in the emerging field of immuno-oncology, to develop novel engineered T cell therapies for cancer, which Juno Therapeutics and we amended and restated in May 2018. In March 2017, we entered into a strategic alliance and option agreement with 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. In July 2018, Allergan exercised its option to develop and commercialize EDIT-101 and paid us $15.0 million in connection with such exercise (the "EDIT-101 Option Exercise Payment"). We and an affiliate of Allergan subsequently entered into a co-development and commercialization agreement under which we will co-develop and equally split profits and losses for EDIT-101 in the United States. In December 2018, we also received a $25.0 million payment from Allergan in connection with the acceptance of the IND for EDIT-101 (the "EDIT-101 Milestone Payment").

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. Except for EDIT-101, all of our research programs are still in the preclinical or research stage of development and the risk of failure of all of our research programs 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 at-the-market offerings, private placements of our preferred stock, payments received under our collaboration with Juno Therapeutics and payments received under our strategic alliance with Allergan. From inception through December 31, 2018, we raised an aggregate of $674.2 million to fund our operations.

Since inception, we have incurred significant operating losses. Our net losses were $110.0 million, $120.3 million and $97.2 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, we had an accumulated deficit of $416.3 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; prepare for and initiate clinical development of EDIT-101 to treat LCA10; 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, 2019 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 May 2018, in connection with the amendment and restatement of our collaboration agreement with Juno Therapeutics to expand our collaboration to add an additional research program, we received $5.0 million for amending the agreement and two $2.5 million milestone payments for technical progress in a research program (the "Juno Therapeutics Amendment Payments"). In addition, we will receive up to $22.0 million in research support over the five years of the collaboration and across the four programs under the collaboration, subject to adjustment in accordance with the terms of the agreement. Through December 31, 2018, we had recognized an aggregate of $17.7 million of research support from Juno Therapeutics since entering into the collaboration. During the year ended December 31, 2018, we recognized $6.4 million of research support from Juno Therapeutics. As of December 31, 2018, we recorded $32.0 million of deferred revenue, $29.2 million of which is classified as long-term on our consolidated

balance sheet, related to 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"). In addition, we received $15.0 million related to the EDIT-101 Option Exercise Payment in July 2018 and $25.0 million related to the EDIT-101 Milestone Payment in December 2018. Through December 31, 2018, we had recognized an aggregate of $30.8 million in revenue related to our strategic alliance with Allergan, which includes all of the EDIT-101 Option Exercise Payment and a portion of the EDIT-101 Milestone Payment. For the year ended December 31, 2018, we recognized $21.5 million in revenue in connection with the Allergan Upfront, which includes all of the EDIT-101 Option Exercise Payment and a portion of the EDIT-101 Milestone Payment. As of December 31, 2018, we recorded $99.2 million of deferred revenue, of which $86.4 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 alliance with Allergan, 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 and development 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. As a result of Allergan's exercise of its option to license EDIT-101 and our election to enter into a profit-sharing arrangement with Allergan in the United States for EDIT-101, our obligations to fund such program in the United States will represent 50% of the total costs related to developing and commercializing the program in the United States.

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 prepare for and initiate the clinical development for EDIT-101, as well as supporting preclinical studies for 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 intellectual property 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 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 expenses associated with operating as 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 intellectual property-related expenses specifically, given the ongoing nature of the 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"), we anticipate general and administrative expenses will continue to be significant. Some of our in-licensed patents and patent applications 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 disputes during future periods will be substantial until such proceedings are resolved.

Other Income (Expense), Net

For the year ended December 31, 2018, other income, net consisted primarily of interest income, accretion of discounts associated with marketable securities, and rental income from our former subtenant, partially offset by interest expense on our construction financing lease obligation.

For the year ended December 31, 2017, other expense, net consisted 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 former subtenant, interest income, and accretion of discounts associated with marketable securities.

For the year ended December 31, 2016, other income, net consisted primarily of 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.

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

We recognize revenue in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC"), Topic 606, *Revenue Recognition* ("ASC 606"). Accordingly, we recognize revenue following the five step model prescribed under Accounting Standards Updates No. 2014-09, *Revenue from Contracts with Customers*: (i) identify contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenues when (or as) we satisfy the performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract and determine those that are performance obligations, and whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

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

Accrued Research and Development Expenses

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

expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

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

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

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,		
	2018	2017	2016
Expected volatility	77.5 %	77.8 %	78.4 %
Expected term (in years)	6.25	6.25	6.25
Risk-free interest rate	2.9 %	2.1 %	1.5 %
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 were as follows. There were no stock options granted to non-employees during 2017 or 2018:

	Year Ended December 31,		
	2018	2017	2016
Expected volatility	—	—	76.5 %
Expected term (in years)	—	—	10.0
Risk-free interest rate	—	—	1.6 %
Expected dividend yield	—	—	—

Stock-based compensation totaled approximately $26.6 million, $23.4 million and $16.9 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, we had $6.0 million and $47.4 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 3.7 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.

Corporate Equity Securities

We record investments in privately issued corporate equity securities that do not have readily determinable fair values at cost and adjust for changes in observable prices minus impairment. Each reporting period we adjust the carrying value of these investments if we observe that additional shares have been issued in an orderly transaction between market participants resulting in a price increase or decrease per share. Additionally, each reporting period we review these investments for impairment considering all available information to conclude whether an impairment exists. Changes in measurement for all corporate equity investments are recognized in “Other income (expense), net.”

Results of Operations

Comparison of Years ended December 31, 2018 and 2017

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017, together with the changes in those items in dollars (in thousands) and the respective percentages of change:

	Year Ended December 31,			
	2018	2017	Dollar Change	Percentage Change
Collaboration and other research and development revenues	$ 31,937	$ 13,728	$ 18,209	n/m
Operating expenses:				
Research and development	90,654	83,159	7,495	9 %
General and administrative	55,010	50,502	4,508	9 %
Total operating expenses	145,664	133,661	12,003	9 %
Other income (expense), net				
Other income, net	328	587	(259)	(44)%
Interest income (expense), net	3,445	(978)	4,423	n/m
Total other income (expense), net	3,773	(391)	4,164	n/m
Net loss	$ (109,954)	$ (120,324)	$ 10,370	9 %

For our results of operations, we have included the respective percentage of changes, unless greater than 100% or less than (100)%, in which case we have denoted such changes as not meaningful (n/m).

Collaboration and Other Research and Development Revenues

Collaboration and other research and development revenues increased by $18.2 million, to $31.9 million for the year ended December 31, 2018 from $13.7 million for the year ended December 31, 2017. This increase was primarily attributable to a $12.7 million increase in revenue recognized pursuant to our strategic alliance with Allergan, $4.0 million in revenue recognized in connection with entering into a license agreement with Beam Therapeutics Inc. (“Beam”) and a $1.5 million increase in revenue recognized pursuant to our collaboration agreement with Juno Therapeutics.

Research and Development Expenses

Research and development expenses increased by $7.5 million, to $90.7 million for the year ended December 31, 2018 from $83.2 million for the year ended December 31, 2017. The following table summarizes our research and development expenses for the years ended December 31, 2018 and December 31, 2017, together with the changes in those items in dollars (in thousands) and the respective percentages of change:

	Year Ended December 31,			
	2018	2017	Dollar Change	Percentage Change
Process and platform development expenses	$ 25,466	$ 17,117	$ 8,349	49 %
Employee related expenses	19,771	14,406	5,365	37 %
Stock-based compensation expenses	14,734	15,131	(397)	(3)%
Success payment expenses	12,500	14,500	(2,000)	(14)%
Licensing and sublicensing payment expenses	8,707	14,610	(5,903)	(40)%
Facility expenses	6,058	4,416	1,642	37 %
Other expenses	3,418	2,979	439	15 %
Total research and development expenses	$ 90,654	$ 83,159	$ 7,495	9 %

The increase in research and development expenses for the year ended December 31, 2018 compared to the year ended December 31, 2017 was primarily attributable to:

- approximately $8.3 million in increased process and platform development expenses due to increased research activity, mostly relating to external research and development costs that we expect will increase further as we continue to prepare for and initiate clinical development for EDIT-101, which was partially offset by $1.7 million in reimbursable research and development expenses associated with our profit-sharing arrangement with Allergan related to EDIT-101;

- approximately $5.4 million in increased employee related expenses due to an increase in the size of our workforce; and

- approximately $2.0 million in increased facility and other related expenses due to increased professional service and office expenses.

These increases were partially offset by the following decreases in research and development expenses:

- approximately $5.9 million in decreased licensing and sublicensing payment expenses resulting primarily from $14.5 million in sublicense fees that were owed to certain of our licensors in connection with receiving the Allergan Upfront and a milestone received under our collaboration with Juno Therapeutics in 2017, partially offset by $8.2 million in sublicense fees owed to certain of our licensors in connection with the EDIT-101 Option Exercise Payment, EDIT-101 Milestone Payment, certain amendment and milestone payments received from Juno Therapeutics under our collaboration and the consideration received from Beam in connection with entering into a license agreement in 2018;

- approximately $2.0 million in decreased success payment expenses resulting primarily from $14.5 million in 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”) in 2017, partially offset by the $12.5 million notes payable that were issued to Broad and settled during the second quarter of 2018 in connection with us entering into a sponsored research agreement with Broad; and

- approximately $0.4 million in decreased stock-based compensation expenses.

General and Administrative Expenses

General and administrative expenses increased by $4.5 million, to $55.0 million for the year ended December 31, 2018 from $50.5 million for the year ended December 31, 2017. The following table summarizes our general and administrative expenses for the years ended December 31, 2018 and December 31, 2017, together with the changes in those items in dollars (in thousands) and the respective percentages of change:

	Year Ended December 31,			
	2018	2017	Dollar Change	Percentage Change
Intellectual property and patent related fees	$ 20,442	$ 23,921	$ (3,479)	(15)%
Stock-based compensation expenses	11,864	8,233	3,631	44 %
Employee related expenses	11,502	8,915	2,587	29 %
Professional service expenses	6,875	6,010	865	14 %
Other expenses	4,327	3,423	904	26 %
Total general and administrative expenses	$ 55,010	$ 50,502	$ 4,508	9 %

The increase in general and administrative expenses for the year ended December 31, 2018 compared to the year ended December 31, 2017 was primarily attributable to:

- approximately $3.6 million in increased stock-based compensation expenses due to an increase in employee stock option expense;
- approximately $2.6 million in increased employee related expenses due to an increase in the size of our workforce;
- approximately $0.9 million in increased other expenses including facility-related expenses; and
- approximately $0.9 million in increased professional services expenses.

These increases were partially offset by an approximate $3.5 million in decreased intellectual property and patent related fees, including expenses associated with the prosecution and maintenance of patents and patent applications.

Other Income (Expense), Net

For the year ended December 31, 2018, other income, net was $3.8 million, which was primarily attributable to interest income, accretion of discounts associated with marketable securities, and rental income from our former subtenant, partially offset by interest expense on our construction financing lease obligation.

For the year ended December 31, 2017, other expense, net was $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 former subtenant, interest income and accretion of discounts associated with marketable securities.

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:

	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 (expense) income, net:				
Other income (expense), net	587	(57)	644	n/m
Interest income (expense), net	(978)	62	(1,040)	n/m
Total other income (expense), 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 increased by $7.7 million, to $13.7 million for the year ended December 31, 2017 from $6.1 million for year ended December 31, 2016. This increase was primarily attributable to $8.8 million in revenue recognized pursuant to our strategic alliance with Allergan, partially offset by a $0.8 million decrease in revenue recognized pursuant to our collaboration agreement with Juno Therapeutics.

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	n/m
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 MGH;
- approximately $7.5 million in increased process and platform development expenses due to increased research activity;
- 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 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 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
Intellectual property and patent related fees	$ 23,921	$ 26,963	$ (3,042)	(11)%
Employee related expenses	8,915	6,881	2,034	30 %
Stock-based compensation expenses	8,233	4,234	3,999	94 %
Professional service expenses	6,010	5,483	527	10 %
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 expense, net was $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 former subtenant, interest income and accretion of discounts associated with marketable securities.

For the year ended December 31, 2016, other income, net was $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.

Liquidity and Capital Resources

Sources of Liquidity

From inception through December 31, 2018, we funded our operations primarily through proceeds from private placements of our preferred stock of $163.3 million, net proceeds of $328.3 million from public offerings of our common stock, the Allergan Upfront and other milestones paid by Allergan, and payments from Juno Therapeutics under our collaboration with them. As of December 31, 2018, we had cash, cash equivalents and marketable securities of $369.0 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, certain cost reimbursement for EDIT-101 costs in the United States and certain option exercise or extension 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 and, as such, are uncertain at this time. As of December 31, 2018, our right to contingent payments under our collaboration agreement with Juno Therapeutics and our strategic alliance with Allergan are our only significant committed potential external sources of funds.

At-the-Market Offerings

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 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. In March 2018, we entered into a sales agreement with Cowen, under which we are able from time to time to issue and sell shares of our common stock through Cowen for aggregate gross sales proceeds of $150.0 million. In November 2018, we sold 1,107,000 shares of our common stock to Cowen at a weighted-average price of $26.95 per share (the "November Offering"). We paid a 3% cash commission on the gross sales price per share of common stock sold resulting in our receiving net proceeds of $28.4 million.

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. In June 2018, in connection with entering into a sponsored research agreement with Broad, we issued promissory notes to Broad in the aggregate original principal amount of $12.5 million and issued 330,617 shares of our common stock to the Broad as payment of all outstanding principal and interest under such notes. Upon such issuance, such notes were cancelled.

Under the terms of the Cpf1 License Agreement, Cas9-II License Agreement and our sponsored research agreement with Broad, 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, 2018, 2017 and 2016, respectively (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Net cash (used in) provided by:			
Operating activities	$ (45,707)	$ (9,417)	$ (50,246)
Investing activities	(53,087)	(183,810)	(3,473)
Financing activities	86,940	154,534	97,161
Net increase (decrease) in cash and cash equivalents	$ (11,854)	$ (38,693)	$ 43,442

Net Cash Used in Operating Activities

Net cash used in operating activities was approximately $45.7 million for the year ended December 31, 2018, and consisted primarily of a net loss of $110.0 million adjusted for non-cash items, including non-cash research and development expenses of $14.4 million, stock-based compensation expenses of $26.6 million, non-cash investment income from corporate equity securities of $3.7 million, depreciation expense of $3.3 million, other non-cash items income of $3.3 million and a net change in operating assets and liabilities of $26.9 million. The change in operating assets and liabilities was related to an increase in deferred revenue of $22.9 million, an increase in accrued expenses of $4.0 million, an increase in accounts payable of $1.8 million, an increase in other current liabilities of $1.0 million and a decrease in accounts receivable of $0.6 million, partially offset by an increase in prepaid expenses and other current assets of $3.4 million and an increase in other non-current assets of $0.1 million.

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 Investing Activities

Net cash used in investing activities was approximately $53.1 million for the year ended December 31, 2018 and consisted primarily of costs to acquire marketable securities of $459.4 million and costs to acquire property plant and equipment of $4.8 million, partially offset by proceeds from maturities of marketable securities of $411.0 million.

Net cash used in investing activities was approximately $183.8 million for the year ended December 31, 2017, and consisted primarily of costs to acquire marketable securities of $375.3 million and costs to acquire property plant and 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 costs to acquire property plant and equipment.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was approximately $86.9 million for the year ended December 31, 2018, primarily related to $76.8 million in proceeds received from at-the-market offerings of our common stock, net of issuance costs that were paid as of December 31, 2018, $10.3 million in proceeds from exercises of options for our common stock and $0.7 million from issuances of our common stock under benefit plans, partially offset by payments on our construction financing lease obligation of $0.9 million.

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 lease 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 exercises of options for our common stock of $0.2 million, partially offset by payments on our construction financing lease obligation of $0.6 million.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we continue to advance our current research programs and our preclinical development activities; prepare for and initiate the clinical development of EDIT-101 to treat LCA10; 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 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. 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, since 2016 we have 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, 2018 and anticipated interest income 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 for and initiating the clinical development of EDIT-101 to treat LCA10;
- 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 additional 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, 2018 (in thousands):

	Total	Less Than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
Sublicensing expenses [1]	$ 3,750	$ 3,750	$ —	$ —	$ —
Operating lease obligations [2]	24,129	5,477	14,850	3,802	—
Total	$ 27,879	$ 9,227	$ 14,850	$ 3,802	$ —

(1) In January 2019, we settled the contractual obligation in cash related to $3.8 million in sublicense fees owed to certain of our licensors in connection with the EDIT-101 Milestone Payment.

(2) Represents future minimum lease payments under our non-cancelable operating leases. The minimum lease payments above exclude our share of the facility operating expenses and other costs that are reimbursable to the landlord under the leases.

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.”

We enter into contracts in the normal course of business with contract research organizations and other vendors 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, 2018, 2017 and 2016.

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, 2018, we had cash and cash equivalents of $134.8 million, primarily held in money market mutual funds consisting of U.S. government-backed securities, and marketable securities of $234.2 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, 2018 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, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, redeemable convertible preferred stock and stockholders' (deficit) equity, and cash flows for each of the three years in the period ended December 31, 2018, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 28, 2019 expressed an unqualified opinion thereon.

Adoption of ASU No. 2014-09

As discussed in Note 1 to the consolidated financial statements, the Company changed its method of accounting for revenue in 2018 due to the adoption of Accounting Standards Update (ASU) No. 2014-09, Revenue from Contracts with Customers (Topic 606), and the related amendments.

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 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. 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
February 28, 2019

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

	December 31, 2018	December 31, 2017
ASSETS		
Current assets:		
Cash and cash equivalents	$ 134,776	$ 146,630
Marketable securities	234,179	182,509
Accounts receivable	30	679
Prepaid expenses and other current assets	5,791	2,381
Total current assets	374,776	332,199
Property and equipment, net	40,232	39,442
Restricted cash and other non-current assets	5,378	1,619
Total assets	$ 420,386	$ 373,260
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 5,327	$ 4,020
Accrued expenses	12,813	11,049
Notes payable	—	7,500
Deferred revenue, current	15,712	13,238
Other current liabilities	2,048	900
Total current liabilities	35,900	36,707
Deferred revenue, net of current portion	115,614	94,725
Construction financing lease obligation, net of current portion	32,417	33,431
Other non-current liabilities	293	317
Total liabilities	184,224	165,180
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; 49,028,907 and 45,025,448 shares issued, and 48,758,951 and 44,507,960 shares outstanding at December 31, 2018 and December 31, 2017, respectively	5	4
Additional paid-in capital	652,464	514,002
Accumulated other comprehensive loss	(29)	(76)
Accumulated deficit	(416,278)	(305,850)
Total stockholders' equity	236,162	208,080
Total liabilities and stockholders' equity	$ 420,386	$ 373,260

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,		
	2018	2017	2016
Collaboration and other research and development revenues	$ 31,937	$ 13,728	$ 6,053
Operating expenses:			
Research and development	90,654	83,159	56,979
General and administrative	55,010	50,502	46,262
Total operating expenses	145,664	133,661	103,241
Operating loss	(113,727)	(119,933)	(97,188)
Other income (expense), net			
Other income (expense), net	328	587	(57)
Interest income (expense), net	3,445	(978)	62
Total other income (expense), net	3,773	(391)	5
Net loss	$ (109,954)	$ (120,324)	$ (97,183)
Reconciliation of net loss to net loss attributable to common stockholders:			
Net loss	$ (109,954)	$ (120,324)	$ (97,183)
Accretion of redeemable convertible preferred stock to redemption value	—	—	(47)
Net loss attributable to common stockholders	$ (109,954)	$ (120,324)	$ (97,230)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.33)	$ (2.98)	$ (3.02)
Weighted-average common shares outstanding, basic and diluted	47,097,735	40,323,631	32,219,717

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,		
	2018	2017	2016
Net Loss	$ (109,954)	$ (120,324)	$ (97,183)
Other comprehensive loss:			
Unrealized loss on marketable securities	47	(76)	—
Comprehensive loss	$ (109,907)	$ (120,400)	$ (97,183)

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

Editas Medicine, Inc.
Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' (Deficit) Equity
(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, 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
Cumulative effect adjustment for adoption of new accounting guidance	—	—	—	—	—	(474)	—	(474)
Issuance of common stock for repayment of notes payable	—	—	636,526	—	22,030	—	—	22,030
Issuance of common stock from public offering, net of issuance costs of $0.1 million	—	—	1,429,205	1	48,493	—	—	48,494
Issuance of common stock from public offering, net of issuance costs of $0.6 million	—	—	1,107,000	—	28,387	—	—	28,387
Issuance of common stock for asset purchase agreement	—	—	56,099	—	1,942	—	—	1,942
Exercise of stock options	—	—	749,294	—	10,328	—	—	10,328
Stock-based compensation expense	—	—	—	—	24,180	—	—	24,180
Purchase of common stock under benefits plans	—	—	26,272	—	680	—	—	680
Vesting of founder shares	—	—	72,000	—	2,418	—	—	2,418
Vesting of employee restricted common stock and common stock subject to repurchase	—	—	174,595	—	4	—	—	4
Unrealized losses on marketable securities	—	—	—	—	—	—	47	47
Net loss	—	—	—	—	—	(109,954)	—	(109,954)
Balance at December 31, 2018	—	$ —	48,758,951	$ 5	$ 652,464	$ (416,278)	$ (29)	$ 236,162

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,		
	2018	2017	2016
Cash flow from operating activities			
Net loss	$ (109,954)	$ (120,324)	$ (97,183)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	26,598	23,364	16,881
Depreciation	3,254	2,683	1,202
Non-cash research and development expenses	14,442	14,500	10,000
Re-measurement of warrant to purchase redeemable securities	—	—	87
Non-cash investment in equity securities	(3,667)	—	—
Other non-cash items, net	(3,268)	(300)	869
Changes in operating assets and liabilities:			
Accounts receivable	649	(591)	931
Prepaid expenses and other current assets	(3,410)	(596)	(1,306)
Other non-current assets	(92)	2	2,246
Accounts payable	1,780	(1,515)	3,251
Accrued expenses	4,042	(8,334)	11,841
Deferred revenue	22,889	81,707	935
Other current and non-current liabilities	1,030	(13)	—
Net cash used in operating activities	(45,707)	(9,417)	(50,246)
Cash flow from investing activities			
Purchases of property and equipment	(4,754)	(2,059)	(3,493)
Proceeds from the sale of equipment	37	15	20
Purchases of marketable securities	(459,370)	(375,266)	—
Proceeds from maturities of marketable securities	411,000	193,500	—
Net cash used in investing activities	(53,087)	(183,810)	(3,473)
Cash flow from financing activities			
Proceeds from offering of common stock, net of issuance costs	76,789	154,143	97,488
Proceeds from exercise of stock options	10,328	1,755	233
Payments on construction financing lease obligation	(857)	(764)	(560)
Issuances of common stock under benefit plans	680	—	—
Payments of notes payable	—	(600)	—
Net cash provided by financing activities	86,940	154,534	97,161
Net increase (decrease) in cash, cash equivalents, and restricted cash	(11,854)	(38,693)	43,442
Cash, cash equivalents, and restricted cash, beginning of period	148,249	186,942	143,500
Cash, cash equivalents, and restricted cash, end of period	$ 136,395	$ 148,249	$ 186,942
Supplemental disclosure of cash and non-cash activities:			
Accretion of redeemable convertible preferred stock to redemption value	$ —	$ —	$ 47
Fixed asset additions included in accounts payable and accrued expenses	659	623	130
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	4	11	11
Offering expenses included in accounts payable and accrued expenses	92	235	—
Issuance of common stock for repayment of notes payable	22,030	14,823	—
Issuance of common stock for asset acquisition	1,942	—	—

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 clinical stage company dedicated to treating patients with genetically addressable diseases. 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, its at-the-market offerings of its common stock in January 2018 and November 2018, and private placements of preferred stock, payments received under a research collaboration with Juno Therapeutics, Inc., a Celgene company that is a wholly-owned subsidiary of Celgene Corporation ("Juno Therapeutics"), and from payments received 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 and received aggregate net proceeds of approximately $97.5 million. In March 2017, the Company completed a follow-on offering and received net proceeds of approximately $96.7 million (the "2017 March Offering"). In December 2017, the Company completed another follow-on offering and received net proceeds of approximately $57.2 million (the "2017 December Offering"). The Company completed at-the-market offerings in January 2018, receiving net proceeds of approximately $48.5 million (the "January 2018 ATM Offering"), and an at-the-market offering November 2018, receiving net proceeds of approximately $28.4 million (the "November 2018 ATM Offering").

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, 2018 and anticipated interest income 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 $416.3 million at December 31, 2018, 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 and deferred tax valuation allowances. 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 held in the form of money market accounts as collateral for the Company's construction financing lease obligation as of December 31, 2018, 2017 and 2016.

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,		
	2018	2017	2016
Cash and cash equivalents	$ 134,776	$ 146,630	$ 185,323
Restricted cash included in "Restricted cash and other non-current assets"	1,619	1,619	1,619
Total	$ 136,395	$ 148,249	$ 186,942

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, 2018 and 2017.

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, 2018.

Revenue Recognition

To date, the Company has primarily earned revenue under the collaboration and license agreement with Juno Therapeutics and the strategic alliance with Allergan.

The Company recognizes revenue in accordance with ASC Topic 606, *Revenue from Contracts with Customers* (“ASC 606”), effective January 1, 2018. The Company enters into collaboration agreements and certain other agreements that are within the scope of ASC 606, under which the Company licenses, may license or grants an option to license rights to certain of the Company’s product candidates and performs research and development services in connection with such arrangements. The terms of these arrangements typically include payment of one or more of the following: non-refundable, up-front fees; reimbursement of research and development costs; development, clinical, regulatory and commercial sales milestone payments, and royalties on net sales of licensed products.

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine the appropriate amount of revenue to be recognized for arrangements determined to be within the scope of ASC 606, the Company performs the following five steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect consideration it is entitled to in exchange for the goods or services it transfers to the customer.

The promised goods or services in the Company’s arrangements typically consist of a license, or option to license, rights to the Company’s intellectual property or research and development services. The Company provides options to additional items in such arrangements, which are accounted for as separate contracts when the customer elects to exercise such options, unless the option provides a material right to the customer. Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer and are considered distinct when (i) the customer can benefit from the good or service on its own or together with other readily available resources

and (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised good or services are distinct, the Company considers factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on its own or whether the required expertise is readily available and whether the goods or services are integral or dependent to other goods or services in the contract.

The Company estimates the transaction price based on the amount expected to be received for transferring the promised goods or services in the contract. The consideration may include fixed consideration or variable consideration. At the inception of each arrangement that includes variable consideration, the Company evaluates the amount of potential payment and the likelihood that the payments will be received. The Company utilizes either the most likely amount method or expected value method to estimate the amount expected to be received based on which method best predicts the amount expected to be received. The amount of variable consideration that is included in the transaction price may be constrained and is included in the transaction price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period.

The Company's contracts often include development and regulatory milestone payments that are as assessed under the most likely amount method and constrained if it is probable that a significant revenue reversal would occur. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, the Company re-evaluates the probability of achievement of such development and clinical milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration and other research and development revenues in the period of adjustment.

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of the Company's collaboration or strategic alliance arrangements.

The Company allocates the transaction price based on the estimated standalone selling price. The Company must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. The Company utilizes key assumptions to determine the stand-alone selling price, which may include other comparable transactions, pricing considered in negotiating the transaction and the estimated costs. Variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated are consistent with the amounts the Company would expect to receive for the satisfaction of each performance obligation.

The consideration allocated to each performance obligation is recognized as revenue when control is transferred for the related goods or services. For performance obligations which consist of licenses and other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

The Company receives payments from its customers based on billing schedules established in each contract. Up-front payments and fees are recorded as deferred revenue upon receipt or when due until the Company performs its obligations under these arrangements. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional.

Prior to ASC 606 Adoption

Revenue for the years ended December 31, 2017 and 2016 were recognized in accordance with ASC Topic 605, *Revenue Recognition* ("ASC 605"). Accordingly, revenue was 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 were 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 evaluated 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 evaluated multiple-element arrangements to determine (1) the deliverables included in the arrangement and (2) whether the individual deliverables represented separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involved subjective determinations and required the Company to make judgments about the individual deliverables and whether such deliverables were separable from the other aspects of the contractual relationship. Deliverables were considered separate units of accounting provided that the delivered item had value to the customer on a standalone basis and, if the arrangement included 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 had standalone value, the Company considered 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 considered 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 were considered substantive if, at the inception of the arrangement, the Company was at risk as to whether the collaboration partner will choose to exercise the option. Factors that the Company considered 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 was 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 was then allocated among the separate units of accounting using the relative selling price method. The Company determined 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 required significant judgment. In developing the BESP for a unit of accounting, the Company considered 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 validated the BESP for units of accounting by evaluating whether changes in the key assumptions used to determine the BESP had a significant effect on the allocation of arrangement consideration between multiple units of accounting.

The Company recognized 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 recognized 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 recognized 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 recognized 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 evaluated whether each milestone was 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 evaluated 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 was 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 were 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.

Research and Development Expenses

Research and development expenses 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 and clinical activities on the Company's behalf, the cost of purchasing lab supplies and non-capital equipment used in preclinical and clinical activities and in manufacturing preclinical and clinical 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 in-licenses, as incurred and classifies such costs as general and administrative expenses in the accompanying consolidated 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 the Company 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 consolidated balance sheet at its historical cost, and such asset would be depreciated over its estimated useful life of thirty years.

Operating Lease Obligations

Operating lease obligations represent future minimum lease payments under the Company's non-cancelable operating leases. The minimum lease payments exclude the Company's share of the facility operating expenses and other costs that are reimbursable to the landlord under the leases. The Company enters into contracts in the normal course of business with contract research organizations and other vendors to assist in the performance of its 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.

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.

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

For the years ended December 31, 2018 and 2017, 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 former 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.

Corporate Equity Securities

The Company records investments in privately issued corporate equity securities that do not have readily determinable fair values at cost and adjusts for changes in observable prices minus impairment. Each reporting period the Company adjusts the carrying value of these investments if it observes that additional shares have been issued in an orderly transaction between market participants resulting in a price increase or decrease per share. Additionally, each reporting period the Company reviews these investments for impairment considering all available information to conclude whether an impairment exists. Changes in measurement for all corporate equity investments are recognized in "Other income (expense), net."

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 for which the Company does not obtain collateral. As of December 31, 2018, 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 - Adopted

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. The guidance is effective on a retrospective basis. The Company adopted 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. 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,		
	2018	2017	2016
Cash and cash equivalents	$ 134,776	$ 146,630	$ 185,323
Restricted cash included in "Restricted cash and other non-current assets"	1,619	1,619	1,619
Total	$ 136,395	$ 148,249	$ 186,942

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers*, which supersedes the revenue recognition requirements in FASB ASC Topic 605, *Revenue Recognition*, and most industry-specific guidance. The Company adopted the new standard effective January 1, 2018 using the modified retrospective approach. As part of the adoption, the Company reviewed all contracts that were not yet completed as of the date of initial application in determining the cumulative-effect impact related to the adoption of ASC 606. The adoption of ASC 606 resulted in the changes to (i) the allocation of arrangement consideration, including the determination of estimated selling price and the allocation of variable consideration to specific performance obligations for the Company's collaboration agreement with Juno Therapeutics, and (ii) the application of proportional performance as a measure of progress on service related deliverables for the Company's strategic alliance with Allergan.

Effective January 1, 2018, the Company's adoption of ASC 606 resulted in increases of $0.5 million in deferred revenue and accumulated deficit, which was primarily due to an adjustment for two milestone payments previously earned that will now be recognized over time, partially offset by acceleration of proportional performance revenue.

The following table presents changes in the Company's deferred revenue balance as of January 1, 2018 resulting from adoption of ASC 606 (in thousands):

	Balance at December 31, 2017	Adjustments	Balance at January 1, 2018
Contract liabilities:			
Deferred revenue	$ (107,963)	$ (474)	$ (108,437)

As of December 31, 2018, the Company's accounts receivable and contract liabilities were primarily related to the Company's collaboration with Juno Therapeutics and strategic alliance Allergan. The following table presents changes in the Company's accounts receivable and contract liabilities for the year ended December 31, 2018 (in thousands):

For the year ended December 31, 2018	Balance at December 31, 2017	Additions	Deductions	Balance at December 31, 2018
Accounts receivable	$ 679	$ 1,189	$ (1,838)	$ 30
Contract liabilities:				
Deferred revenue	$ (107,963)	$ (31,497)	$ 8,134	$ (131,326)

During the three months and year ended December 31, 2018, the Company recognized revenue as a result of the following (in thousands):

	Three Months Ended	Year Ended
	December 31, 2018	
Revenue recognized in the period from:		
Amounts included in deferred revenue at the beginning of the period	$ 1,417	$ 5,874
Performance obligations satisfied in previous periods	$ 4,645	$ 5,956

For additional information regarding revenue recognition from contracts with customers, refer to Note 9.

The Company has included the following financial statement line items for comparability purposes as of and for the three months and year ended December 31, 2018 (in thousands, except per share data):

	Three Months Ended December 31, 2018		
	As reported under Topic 606	Balances without adoption of ASC 606	Effect of Change
Collaboration and other research and development revenues	$ 6,119	$ 5,060	$ 1,059
Operating loss	$ (26,253)	$ (27,312)	$ 1,059
Net loss attributable to common stockholders	$ (25,054)	$ (26,113)	$ 1,059
Net loss per share attributable to common stockholders, basic and diluted	$ (0.52)	$ (0.54)	$ 0.02

	Year Ended December 31, 2018		
	As reported under Topic 606	Balances without adoption of ASC 606	Effect of Change
Collaboration and other research and development revenues	$ 31,937	$ 33,993	$ (2,056)
Operating loss	$ (113,727)	$ (111,671)	$ (2,056)
Net loss attributable to common stockholders	$ (109,954)	$ (107,898)	$ (2,056)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.33)	$ (2.29)	$ (0.04)

	As of December 31, 2018		
	As reported under Topic 606	Balances without adoption of ASC 606	Effect of Change
Deferred revenue, current	$ (15,712)	$ (17,552)	$ 1,840
Deferred revenue, net of current portion	$ (115,614)	$ (111,466)	$ (4,148)
Accumulated deficit	$ (416,278)	$ (414,222)	$ (2,056)

In 2016, the FASB issued ASU No. 2016-01, *Recognition and Measurement of Financial Assets and Financial Liabilities* ("ASU 2016-01"). ASU 2016-01 amended guidance related to the recording of financial assets and liabilities. Under the amended guidance, equity investments that are not accounted for under the equity method or those that result in the consolidation of an investee, are to be measured at fair value with changes in fair value recognized in net income (loss). An entity has the option to measure equity investments without readily determinable fair values at cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transaction for the identical or similar investments. The amended guidance became effective January 1, 2018. As of December 31, 2018, the Company held an equity investment in Beam Therapeutics Inc. ("Beam"), a privately held company, that it accounted for under the cost method. The equity investment does not have a readily determinable fair value. The Company measured the investment at cost adjusted for impairment or observable price changes. During the year ended December 31, 2018, the Company did not adjust the value of the Company's investment in Beam as a result of impairment or based on observable price changes.

Recent Accounting Pronouncements – Issued But Not Yet Adopted

In February 2016, the FASB issued ASU 2016-02, *Leases* ("ASC 842"), 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, was codified as ASC 842, *Leases*, and amended through subsequent ASUs. ASC 842 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. The Company will recognize a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption, for which comparative periods will be presented in accordance with the previous guidance in ASC 840, *Leases*. The Company has elected, in transition, to apply the package of practical expedients which allows the Company not to reassess whether existing contracts are or contain leases, the classification of existing leases, and whether initial direct costs qualify for capitalization. Additionally, the Company expects to elect the package of practical expedients to: i) not recognize lease assets and lease liabilities for leases with a term of 12 months of less; and ii) not separate the non-lease components from the associated lease components for leases of real estate and, instead, account for each non-lease component and associated lease component as a single component. The Company is evaluating the effect of this guidance on the Company's consolidated financial statements and disclosures, which includes, but is not limited to, the impact on the lease of its corporate headquarters in Cambridge, Massachusetts, and its laboratory space in Boulder, Colorado. The Company currently expects to derecognize the existing asset and liabilities on the consolidated balance sheet resulting from the build-to-suit lease arrangement at the Company's corporate headquarters in Cambridge, Massachusetts, which did not meet the criteria for "sale-leaseback" treatment at the time construction was completed. Also, the Company is in the process of updating its systems, policies and internal controls over financial reporting in anticipation of adopting these standards.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation - Stock Compensation: Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07") to simplify the accounting for share-based payments to non-employees by aligning it with the accounting for share-based payments to employees, with certain exceptions. The new guidance expands the scope of ASC 718, *Compensation – Stock Compensation*, to include share-based payments granted to non-employees in exchange for goods or services used or consumed in an entity's own operations and supersedes the guidance in ASC Topic 505-50, *Equity-Based Payments to Non-Employees*. The guidance is effective for public business entities in annual periods beginning after December 15, 2018 and interim periods within those years. Early adoption is permitted. The Company is currently evaluating the effect of this guidance on the Company's consolidated financial statements and disclosures.

In August 2018, the FASB issued ASU No. 2018-13, *Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"), which modifies certain disclosure requirements on fair value measurements. The amendments regarding changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements and the narrative description of measurement uncertainty are required to be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments are required to be applied retrospectively to all periods presented upon their effective date. ASU 2018-13 is effective for fiscal years beginning after December 15, 2019 and interim periods within those years. The Company does not anticipate a material impact to disclosures as a result of the adoption of ASU 2018-13.

3. Cash Equivalents, Marketable Securities and Corporate Equity Securities

Cash equivalents, marketable securities and corporate equity securities consisted of the following at December 31, 2018 (in thousands):

December 31, 2018	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash equivalents and marketable securities:				
Money market funds	$ 130,049	$ —	$ —	$ 130,049
U.S. Treasuries	208,754	—	(24)	208,730
Government agency securities	29,940	—	(5)	29,935
Equity securities included in other non-current assets:				
Corporate equity securities	3,667	—	—	3,667
Total	$ 372,410	$ —	$ (29)	$ 372,381

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 and marketable securities:				
Money market funds	$ 134,635	$ —	$ —	$ 134,635
U.S. Treasuries	135,601	—	(47)	135,554
Government agency securities	58,979	—	(29)	58,950
Total cash equivalents and marketable securities	$ 329,215	$ —	$ (76)	$ 329,139

At December 31, 2018, the Company held 38 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, 2018 was $210.7 million, and there were no securities held by the Company in an unrealized loss position for more than 12 months. As of December 31, 2018, 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, 2018.

There were no realized gains or losses on available-for-sale securities during the years ended December 31, 2018 or 2017.

4. Fair Value Measurements

Assets measured at fair value on a recurring basis as of December 31, 2018 are as follows (in thousands):

Financial Assets	December 31, 2018	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents:				
Money market funds	$ 130,049	$ 130,049	$ —	$ —
U.S. Treasuries	4,487	4,487	—	—
Marketable securities:				
U.S. Treasuries	204,243	204,243	—	—
Government agency securities	29,935	29,935	—	—
Restricted cash and other non-current assets:				
Corporate equity securities	3,667	—	3,667	—
Money market funds	1,619	1,619	—	—
Total financial assets	$ 374,000	$ 370,333	$ 3,667	$ —

Assets and liabilities 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	$ —	$ —

There were no transfers between fair value measurement levels during the years ended December 31, 2018 or 2017.

5. Prepaid Expenses and Other Current Assets

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

	As of December 31,	
	2018	2017
Prepaid expenses	$ 2,918	$ 1,864
Other	2,873	517
Total	$ 5,791	$ 2,381

6. Property and Equipment, Net

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

	As of December 31,	
	2018	2017
Building	$ 35,167	$ 35,167
Laboratory equipment	10,892	7,415
Computer equipment	733	550
Leasehold improvements	289	177
Furniture and office equipment	166	96
Software	118	95
Total property and equipment	47,365	43,500
Less: accumulated depreciation	(7,133)	(4,058)
Property and equipment, net	$ 40,232	$ 39,442

The Company recorded $3.3 million, $2.7 million and $1.2 million in depreciation expense during the years ended December 31, 2018, 2017 and 2016, respectively.

7. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	As of December 31,	
	2018	2017
Employee related expenses	$ 5,201	$ 3,708
Sublicensing and success payment expenses	3,750	2,000
Intellectual property and patent related fees	1,939	2,370
Process and platform development expenses	1,044	2,301
Professional service expenses	475	487
Other expenses	404	183
Total	$ 12,813	$ 11,049

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 balance sheets as of December 31, 2018 and December 31, 2017.

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

construction financing 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
2019	4,155
2020	4,257
2021	4,362
2022	4,470
2023 (partial year)	3,802
2024 and thereafter	-
Total minimum lease payments	$ 21,046

Rent expense of approximately $1.8 million, $1.2 million and $2.5 million was incurred during the years ended December 31, 2018, 2017 and 2016, respectively.

The Company subleased approximately 10,000 square feet of the Hurley Street premises pursuant to a sublease, which commenced in February 2017 and terminated in June 2018.

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, and other license agreements between the Company and Broad. 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 $14.2 million, $18.2 million and $23.1 million in expense during the years ended December 31, 2018, 2017 and 2016, 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 Company records this expense as a research and development expense in its consolidated 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 $750.0 million. In March 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 another 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. In December 2017, the Company issued promissory notes for an aggregate principal amount of $7.5 million to Broad and settled such notes in January 2018.

The Company triggered a Success Payment under the MGH license agreement during the fourth quarter of 2017 when the Company's market capitalization reached $1.0 billion. The Company accrued $2.0 million relating to the such Success Payment owed to MGH which is included in accrued expense on the consolidated balance sheet for the year ended December 31, 2017. In January 2018, the Company settled this liability through the issuance of 80,000 shares of its common stock to MGH.

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

Research Funding Payments

In June 2018, the Company entered into a sponsored research agreement (the "Sponsored Research Agreement") with Broad, which is described more fully in Note 9. Pursuant to the terms of the Sponsored Research Agreement, the Company is required to make certain research funding payments to Broad, payable by promissory note, cash or common stock. Under the Sponsored Research Agreement, the Company is obligated to make payments of research funding to Broad in the event the Company's market capitalization reaches specified thresholds ranging from a mid-nine digit dollar amount to a low-eleven digit dollar amount ("Market Cap Research Funding") or a Company sale for consideration ranging from a mid-nine digit dollar amount to a low-eleven digit dollar amount ("Company Sale Research Funding" and, collectively with the Market Cap Research Funding, the "Research Funding Payments"). In connection with entering into the Sponsored Research Agreement, the Company confirmed that the first two Research Funding Payments of $5.0 million and $7.5 million were due and payable to Broad (the "Initial Research Payments"). In June 2018, the Company issued promissory notes for an aggregate principal balance of $12.5 million to Broad, which were settled by the issuance of shares of common stock, and are described more fully in the Notes Payable section.

The Research Funding Payments were accounted for under the provisions of FASB ASC, Topic 505-50, Equity-Based Payments to Non-Employees. Other than the Initial Research Payments, the Company is not required to make additional Research Funding Payments if the Company, whether directly or through its affiliates or sublicensees, is not researching, developing, or commercializing products based on or incorporating inventions developed under the Sponsored Research Agreement and exclusively licensed to the Company from Broad or based on or incorporating CRISPR technology owned, co-owned, or controlled by Broad and otherwise licensed to the Company, subject to certain exclusions. As such, the Company will recognize the expenses and liability associated with each Research Funding

Payment upon achievement of the associated Research Funding Payment conditions, if ever. The Company records this expense as a research and development expense in its consolidated statements of operations.

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, the Company 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 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 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 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 were due and payable in May 2018. The December Success Payment Notes were subject to the same interest and terms as the Initial Notes, other than the maturity date. The Company fully settled the outstanding principal and accrued interest on the December Success Payment Notes by issuing 225,909 shares of common stock to Broad in January 2018.

In June 2018, in connection with the Company's entry into the Sponsored Research Agreement and the trigger of the Initial Research Payments, the Company issued promissory notes in an aggregate principal amount of $12.5 million to Broad (the "Initial Research Notes") bearing interest at a rate of 4.8% annum, except with respect to $7.5 million of the principal, which would not start accruing interest until November 2018. The Company fully settled the outstanding principal and accrued interest on the Initial Research Notes by issuing 330,617 shares of common stock to Broad in June 2018.

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, 2018 or 2017.

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 and in May 2018 the Company and Juno Therapeutics entered into an amended and restated collaboration and license agreement (the Collaboration Agreement, as amended and restated, the "Amended

Collaboration Agreement"). 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. Pursuant to the Collaboration Agreement, the parties were pursuing 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, which was increased to four research areas under the Amended Collaboration Agreement.

The collaborative program of research to be undertaken by the parties pursuant to the Amended 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 four 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 four 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"). The Research Program Term and the optional extensions were not changed by the Amended Collaboration Agreement.

Under the terms of the Collaboration Agreement, the Company granted to Juno Therapeutics during the Research Program Term a nonexclusive, worldwide, royalty free, non-sublicensable 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) research, evaluate and conduct preclinical testing and development of certain engineered T cells relating to the three research areas that were originally the subject of the arrangement and (iv) evaluate the data developed in the conduct of activities under the research plan. Pursuant to the terms of the Amended Collaboration Agreement, the license rights granted to Juno Therapeutics were expanded to include, during the Research Program Term, a nonexclusive, worldwide, royalty free, non-sublicensable license under certain of the intellectual property controlled by the Company to: (i) research, evaluate and conduct preclinical testing and development of certain engineered T cells relating to the fourth research area and (ii) research, develop and use certain research tools (together, the initial research license granted per the terms of the Collaboration Agreement and the incremental research license granted per the terms of the Amended Collaboration Agreement, the "Research License").

As it relates to two of the three research areas that were originally the subject of the arrangement, under the terms of the Collaboration Agreement, 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, under the terms of the Collaboration Agreement, the Company granted to Juno Therapeutics a non-exclusive, milestone and royalty bearing, sublicensable 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). Additionally, as it relates to the third research area that was originally the subject of the arrangement, under the terms of the Collaboration Agreement, the Company granted to Juno Therapeutics a 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 or export selected CAR and TCR engineered T cell products that utilize the genome editing reagents generated under the research program associated with those CAR and 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). Pursuant to the terms of the Amended Collaboration Agreement, as it relates to the fourth area of research that was added to the collaboration, the Company granted to Juno Therapeutics a 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 or export selected CAR and TCR engineered T cell products that utilize the genome editing reagents generated under the research program associated with those CAR and 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 fourth 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 fourth research area).

The Amended Collaboration Agreement is being managed on an overall basis by a project leader from each of the Company and Juno Therapeutics. The project leaders serve as the contact point between the parties with respect to the research program and are primarily responsible for facilitating the flow of information, interaction, and collaboration between the parties. In addition, the research and development activities under the Amended Collaboration Agreement during the Research Program Term are governed by a joint research committee ("JRC") formed by an equal number of representatives from the Company and Juno Therapeutics. The JRC oversees, reviews and recommends the direction of the research program. Among other responsibilities, the JRC monitors and reports research progress and ensures open and frequent exchange between the parties regarding research program activities. The Amended Collaboration Agreement did not alter the governance provisions in the Collaboration Agreement.

Under the terms of the Collaboration Agreement, the Company received a $25.0 million up front, non-refundable, non-creditable cash payment. In connection with the entry into the Amended Collaboration Agreement, the Company received an additional $5.0 million up-front, non-refundable, non-creditable cash payment. Moreover, the Company became entitled to receive two $2.5 million milestones related to technical progress in one of the research areas upon the execution of the Amended Collaboration Agreement. 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 four 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 four research areas. Consistent with the terms of the Collaboration Agreement, under the terms of the Amended 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 four research areas. However, for two of the three research areas that were originally the subject of the arrangement, Juno Therapeutics continues to have 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 is 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 that were originally the subject of the arrangement, the Company is eligible to receive up to $77.5 million in development milestone payments and up to $80.0 million in regulatory milestone payments, while the Company is eligible to receive up to $80.0 million in development milestone payments and up to $80.0 million in regulatory milestone payments for the first product to achieve the associated event in the fourth area of research that was added to the collaboration. In addition, the Company is eligible to receive additional development and regulatory milestone payments for subsequent products developed within each of the four 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 four research areas. Development milestone payments are generally 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. The milestone payments and related triggering events associated with the three research areas that were originally the subject of the Collaboration Agreement were not modified in the Amended Collaboration Agreement.

In addition, to the extent any of the product candidates covered by the licenses conveyed to Juno Therapeutics under the Amended Collaboration Agreement are commercialized, the Company would be entitled to receive tiered royalty payments of low double digits based on a percentage of net sales. Similar to the milestones, pursuant to the Amended Collaboration Agreement, the Company is eligible to receive an independent royalty stream associated with the fourth area of research that was added to the collaboration. 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 and July 2017 (the "July 2017 Juno Milestone Payment"). The Company achieved two additional $2.5 million development milestones under the Amended Collaboration Agreement resulting from technical progress in a research program in May 2018. 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, 2018, the next potential milestone payment that the Company may be entitled to receive under the Amended Collaboration Agreement is a milestone payment of $2.5 million for the achievement of certain development criteria. There are no cancellation, termination or refund provisions in the Amended Collaboration Agreement that contain material financial consequences to the Company.

Unless earlier terminated, the Amended Collaboration Agreement will continue in full force and effect, on a licensed product by licensed 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 Amended 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 Amended 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 Amended Collaboration Agreement for convenience upon not less than six months prior written notice to the Company. The Company may terminate the Amended 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 Amended 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 Amended Collaboration Agreement. If Juno Therapeutics terminates the Amended 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 Amended Collaboration Agreement for convenience or if the Company terminates the Amended Collaboration Agreement as a result of Juno Therapeutics' uncured material breach or default, then the licenses conveyed to Juno Therapeutics will terminate. The Amended Collaboration Agreement did not modify the termination provisions in the Collaboration Agreement.

Accounting Analysis

The Company evaluated the Amended Collaboration Agreement in accordance with the provisions of ASC 606. The Company has accounted for the amendment resulting from the Amended Collaboration Agreement as a modification to the original contract and not as a separate contract. The Company combined the Amended Collaboration Agreement with the Collaboration Agreement because the scope of the arrangement did not solely increase due to the addition of distinct promised goods or services with pricing that reflects the associated standalone selling prices. For the remaining goods and services that are distinct from the goods and services that were transferred on or before the date of the effectiveness of the Amended Collaboration Agreement, the Company has accounted for the modification on a prospective basis as if it were a termination of the existing contract and the creation of a new contract. Conversely, the remaining goods and services that are not distinct from the goods and services that were transferred on or before the date of the effectiveness of the Amended Collaboration Agreement were deemed to form part of a single performance obligation that is partially satisfied so they have been accounted for as part of the existing contract for which an adjustment was recorded on a cumulative catch-up basis at the date of the modification.

The Company has identified the following performance obligations under the combined arrangement: (i) Research License and the related research and development services during the Initial Research Program Term (the “Research License and Related Services”), (ii) four material rights related to the first Development and Commercialization Licenses related to each of the four research areas (each, a “First Development and Commercialization License Material Right”) and (iii) six material rights related to the option to purchase up to three additional Development and Commercialization Licenses for two of the research areas (each, an “Additional Development and Commercialization License Material Right”). Upon exercise of the option to obtain a Development and Commercialization License under any of the four research areas, the Company will provide Juno Therapeutics with a license covering the further development and potential commercialization of the underlying target or product, as applicable. The Company has determined that the ability to obtain Development and Commercialization Licenses under the arrangement represents a material right because Juno Therapeutics is entitled to incremental licenses for additional consideration that represents a significant discount from amounts that would otherwise be offered for the related goods to comparable customers outside of the contract.

The Company has concluded that the Research License is not distinct from the research and development services during the Initial Research Program Term as Juno Therapeutics cannot obtain the benefit of the Research License without the Company performing the research and development services. The services incorporate proprietary technology, unique skills and specialized expertise, particularly as it relates to genome editing technology that is not available in the marketplace. As a result, the Research License, inclusive of the incremental license granted in connection with the Amended Collaboration Agreement, has been combined with the research and development services into a bundled performance obligation. The Company has concluded that the First Development and Commercialization License Material Rights for each respective research area and the Additional Development and Commercialization License Material Rights for the two research areas to which they relate are each a separate performance obligation. These material rights, of which there are ten in total, are distinct from the other performance obligations in the arrangement as they are options in the contract that are not required for Juno Therapeutics to obtain the benefit of the other promised goods and services in the arrangement. Accordingly, in accounting for the modification resulting from the Amended Collaboration Agreement, the Research License and Related Services performance obligation was treated as part of the existing contract, whereas the material right performance obligations were treated as a termination of the existing contract and the creation of a new contract.

As of December 31, 2018, the total transaction price associated with the remaining consideration based on the Amended Collaboration Agreement was determined to be $40.7 million, consisting of: (i) $25.0 million upfront non-refundable, non-creditable cash payment associated with the Collaboration Agreement, (ii) $5.0 million upfront non-refundable, non-creditable cash payment associated with the Amended Collaboration Agreement, (iii) $2.9 million of remaining research and development funding, (iv) $2.7 million of milestone payments received by the Company under the Collaboration Agreement that were not yet recognized as revenue and (v) $5.0 million of milestone payments associated with the execution of the Amended Collaboration Agreement. The research and development funding is being paid by Juno Therapeutics to the Company based on the number of the Company’s full time equivalents of its personnel conducting the research under the Amended Collaboration Agreement. The Company utilizes the most likely amount

method to determine the amount of research and development funding to be received. The Company also utilizes the most likely amount method to estimate any development and regulatory milestone payments to be received. As of December 31, 2018, the only milestones that were included in the transaction price were milestones that had been contractually earned and received. The remaining milestones were fully constrained due to the significant uncertainties surrounding such payments. The Company considers the stage of development and the risks associated with the remaining development required to achieve the milestone, as well as whether the achievement of the milestone is outside the control of the Company or Juno Therapeutics. The outstanding milestone payments were fully constrained as of December 31, 2018, as a result of the uncertainty whether any of the milestones will be achieved. The Company has determined that any commercial milestones and sales-based royalties will be recognized when the related sales occur as they were determined to relate predominantly to the license(s) to be granted and therefore have also been excluded from the transaction price. The Company reevaluates the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur. Through the date of the Amended Collaboration Agreement, the Company had recognized approximately $12.3 million of revenue associated with the Research License and Related Services which was excluded from the modification date transaction price.

The transaction price was allocated to the performance obligations based on the relative estimated standalone selling prices of each performance obligation or, in the case of certain variable consideration, to one or more performance obligations. The estimated standalone selling price for the Research License and Related Services is primarily based on the nature of the services to be performed and estimates of the associated effort and costs of the services, adjusted for a reasonable profit margin that would be expected to be realized under similar contracts. The Company developed the estimated standalone selling price for the material rights based on the difference between the value of the license granted and any additional consideration to be received upon exercise of the underlying option, adjusted for the probability of exercise. The value of the license granted was determined 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 transaction price allocated to each performance obligation as of December 31, 2018 was as follows: (i) Research License and Related Services: $10.7 million, (ii) First Development and Commercialization License Material Right related to the first research area: $3.6 million, (iii) First Development and Commercialization License Material Right related to the second research area: $6.0 million, (iv) First Development and Commercialization License Material Right related to the third research area: $0.1 million, (v) First Development and Commercialization License Material Right related to the fourth research area: $18.3 million, (vi) the first Additional Development and Commercialization License Material Right for the first research area: $0.3 million, (vii) the second Additional Development and Commercialization License Material Right for the first research area: $0.2 million, (viii) the third Additional Development and Commercialization License Material Right for the first research area: $0.1 million, (ix) the first Additional Development and Commercialization License Material Right for the second research area: $0.8 million, (x) the second Additional Development and Commercialization License Material Right for the second research area: $0.5 million, and (xi) the third Additional Development and Commercialization License Material Right for the second research area: $0.3 million.

The Company recognizes revenue related to amounts allocated to the Research License and Related Services as the underlying services are performed using a proportional performance model. The Company measures proportional performance based on full time employee hours relative to projected full time employee hours to complete the research services which best reflects the progress towards satisfaction of the performance obligation. Revenue related to each of the material rights will be recognized upon the earlier of when the respective options are exercised and the Company transfers control of the related license or when the respective options lapse. 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, control is deemed to be transferred upon the designation by Juno Therapeutics of the specific target or product, as applicable, whereupon the license becomes effective upon Juno Therapeutics exercising their option. None of the options associated with the material rights had been exercised or had lapsed as of December 31, 2018.

During the years ended December 31, 2018 and 2017, the Company recognized revenue under the Collaboration Agreement and the Amended Collaboration Agreement totaling approximately $6.4 million and $4.9 million, respectively. Included in the revenue recognized during the year ended December 31, 2018 is approximately $3.0 million of additional revenue related to a cumulative catch-up adjustment associated with the Amended Collaboration Agreement. Included in the revenue recognized during the year ended December 31, 2017 is $2.5 million related to the July 2017 Juno Milestone Payment. No revenue had been recognized through the date of the Amended Collaboration Agreement for the material rights performance obligations and there were no cumulative catch-up adjustments recorded for such performance obligations as a result of the Amended Collaboration Agreement. Amounts allocated to each of the material rights will be recognized as revenue prospectively when the material right has been exercised or when the respective option has lapsed.

The revenue is classified as collaboration and other research and development revenues in the accompanying consolidated statements of operations. As of December 31, 2018 and 2017, there was approximately $32.0 million and $26.4 million of deferred revenue, respectively, related to the Amended Collaboration Agreement and the Collaboration Agreement, respectively, of which $29.2 million and $26.4 million were classified as long-term, respectively, in the accompanying consolidated balance sheets. In addition, as of December 31, 2017, the Company had 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, 2018.

During the year ended December 31, 2018, the Company paid $1.7 million in sublicense fees that were owed to certain of the Company's licensors in connection with the Amended Collaboration Agreement, which the Company recorded as research and development expenses during such period. During the year ended December 31, 2017, the Company paid $0.5 million in sublicense fees that were owed to certain of the Company's licensors in connection with the July 2017 Juno Milestone Payment, which the Company recorded as research and development expenses during such period.

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 congenital amaurosis 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. Allergan will have the ability for a defined period of time ("Initial Option Period") to exercise an option (each, an "Option") to obtain a worldwide 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. In July 2018, Allergan exercised its Option with respect to the LCA10 Program. In connection with such exercise, Allergan paid the Company $15.0 million (the "LCA10 Option Exercise Payment"). Following such exercise, the Company exercised its Profit-Share Election with respect to the LCA10 Program. Following such election, the LCA10 Program became subject to a Profit-Sharing Arrangement and, as of December 31, 2018, the parties have not yet entered into a separate profit-sharing agreement with respect to the Profit-Sharing Arrangement.

The initial term of the Allergan Agreement commenced on March 14, 2017 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 March 2017.

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 December 2018, the Company received a $25.0 million payment from Allergan in connection with the acceptance of the IND for EDIT-101, the Company's experimental therapeutic generated under the LCA10 Program (the "EDIT-101 Milestone Payment").

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

(such right, the “Profit-Share Election,” and such arrangement, a “Profit-Sharing Arrangement”). If the Company elects to participate in a Profit-Sharing Arrangement, which it has for the LCA10 Program, the Company is obligated to reimburse Allergan for half of the United States 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 Arrangement the royalties will only be paid on ex-U.S. 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

Under the Allergan Agreement, the Company has identified a single performance obligation that includes (i) the research and development services during the Research Term (the “Allergan R&D Services”), and (ii) Steering Committee services during the Research Term (the “ASC Services”). The Company has concluded that the Allergan R&D Services is not distinct from the ASC Services during the Research Term. 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 Steering Committee 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 a CDP, the ongoing

evaluation of a 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 and as such, the ASC Services along with the Allergan R&D Services are considered one performance obligation (the "CDP Services"). In addition, the Company has concluded that the option to purchase five development and commercialization licenses is considered a marketing offer as the options did not provide any discounts or other rights that would be considered a material right in the arrangement.

As of January 1, 2018, the date of the initial application of ASC 606 by the Company, the total transaction price was determined to be $90.0 million, consisting solely of the upfront non-refundable, non-creditable cash payment. The Company also utilized the most likely amount method to estimate any development and regulatory milestone payments to be received. As of January 1, 2018, there were no milestones included in the transaction price. The milestones were fully constrained due to the significant uncertainties surrounding such payments. The Company considered the stage of development and the risks associated with the remaining development required to achieve the milestone, as well as whether the achievement of the milestone is outside the control of the Company or Allergan. Upon achievement of the EDIT-101 Milestone Payment, $25.0 million was added to the transaction price in November 2018. As of December 31, 2018, the total transaction price is $115.0 million. The remaining milestone payments were fully constrained, as a result of the uncertainty whether any of the milestones would be achieved, as of December 31, 2018. The Company has determined that any commercial milestones and sales-based royalties will be recognized when the related sales occur and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur.

The Company will recognize revenue related to the CDP Services as the underlying services are performed using a proportional performance model. The Company measures proportional performance based on full time employee hours relative to projected full time employee hours to complete the research service.

During the year ended December 31, 2018, the Company recognized revenue under the Allergan Agreement of approximately $21.5 million, which includes $15.0 million related to the LCA10 Option Exercise Payment. During the year ended December 31, 2017, the Company recognized revenue under the Allergan Agreement of approximately $8.8 million. The LCA10 Option Exercise Payment was recognized upon the grant to Allergan of the right to use intellectual property associated with the development and commercialization license for LCA10 and final decision making authority with respect to the LCA10 Program. As of December 31, 2018 and 2017, there was $99.2 million and $81.2 million of deferred revenue related to the Allergan Agreement, respectively, of which $86.4 million and $68.3 million is classified as long-term on the consolidated balance sheet, respectively.

As part of the Profit-Sharing Arrangement, the Company and Allergan will equally split U.S. profits and losses for the LCA10 Program in the United States and will co-develop the LCA10 Program in the United States. The Company accounts for the Profit-Sharing Arrangement with respect to the LCA10 Program within the scope of ASC Topic 808, *Collaborative Arrangements*, given that both the Company and Allergan are active participants in future research and development activities and both parties are exposed to significant risks and rewards dependent on the commercial success of such activities. During the year ended December 31, 2018, the Company and Allergan incurred $5.9 million in expense associated with the LCA10 Program after the option exercise, of which the Company recognized $1.7 million in contra research and development expenses during such period. The reimbursement of $2.3 million is classified as prepaid expenses and other current assets and the liability of $0.6 million in expenses owed to Allergan is classified as other current liabilities in the consolidated balance sheet as of December 31, 2018.

During the year ended December 31, 2018, the Company incurred $6.0 million in sublicense fees owed to certain of the Company's licensors in connection with the LCA10 Option Exercise Payment and EDIT-101 Milestone Payment, which the Company recorded as research and development expenses during such period, of which $3.8 million were accrued in the consolidated balance sheet as of December 31, 2018. 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.

Broad Sponsored Research Agreement

Summary of Agreement

The Sponsored Research Agreement provides for Broad to conduct research useful or relevant to genome editing in the field of genomic medicines for the prevention or treatment of human disease with funding from the Company. Under the Sponsored Research Agreement, Broad granted to the Company an exclusive right of first negotiation for licenses from Broad with respect to patentable inventions developed by Broad in the course of the sponsored research, subject to certain limitations and retained rights ("Sponsored Invention Licenses").

Under the Sponsored Research Agreement, the Company is obligated to make Market Cap Research Funding payments in the event the Company's market capitalization reaches specified thresholds ranging from a mid-nine digit dollar amount to a low-eleven digit dollar amount or Company Sale Research Funding payments in the event of a Company sale for consideration ranging from a mid-nine digit dollar amount to a low-eleven digit dollar amount. In connection with entering into the Sponsored Research Agreement, the Company confirmed that the first two research payments of $5.0 million and $7.5 million, respectively, were due and payable to Broad. In connection with the Initial Research Payments, the Company issued promissory notes to Broad that it settled in common stock in June 2018 as discussed more fully in Note 8. The $12.5 million in research funding expense was recorded to research and development expenses during the year ended December 31, 2018. Other than the Initial Research Payments, the Company is not required to make additional Research Funding Payments if the Company, whether directly or through its affiliates or sublicensees, is not researching, developing, or commercializing products based on or incorporating inventions exclusively licensed to the Company from Broad under Sponsored Invention Licenses or based on or incorporating CRISPR technology owned, co-owned, or controlled by Broad and otherwise licensed to the Company, subject to certain exclusions (an "Applicable Product" and such exemption from payment, the "Funding Exemption"). In the event that the Company, whether directly or through its affiliates or sublicensees, later resumes research, development, or commercialization of an Applicable Product within a specified period of time, any Research Funding Payment that was not paid to Broad as a result of the Funding Exemption shall become payable. Under the Sponsored Research Agreement, the Company is obligated to pay up to $125.0 million to Broad in Research Funding, inclusive of the Initial Research Payments, and in no event shall the aggregate amount of all Research Funding Payments exceed such amount.

Unless the Company has undergone a change in control, Market Cap Research Funding is payable by the Company in cash, common stock, or in the form of promissory notes, which may be settled in shares of common stock at the election of the Company, as discussed more fully in Note 8. Following a change in control of the Company, Company Sale Research Funding is required to be made in cash. The Sponsored Research Agreement is terminable by each party upon the occurrence of specified bankruptcy events of the other party and otherwise will continue in effect until the later of the expenditure of all Research Funding Payments by Broad and such time as the Company has no further rights of first negotiation for Sponsored Invention Licenses, unless otherwise mutually agreed between the parties.

Beam Therapeutics License Agreement

Summary of Agreement

In May 2018, the Company entered into a license agreement with Beam (the "Beam License Agreement"). Beam is a biotechnology company focused on developing precision genetic medicines using technology that converts a single nucleobase into a different nucleobase ("Base Editing"). Pursuant to the Beam License Agreement, the Company granted to Beam licenses and options to acquire licenses to certain intellectual property rights owned or controlled by the Company, for specified uses. More specifically, the Company granted to Beam a worldwide, exclusive (subject to certain exceptions), sublicensable (subject to certain conditions), license under certain intellectual property controlled by the Company for the use of Base Editing therapies for the treatment of any field of human diseases and conditions, subject to certain exceptions (the "Beam Field," and the licenses granted or to be granted under the Beam License Agreement, the "Beam Development and Commercialization License"). Additionally, the Company granted to Beam a royalty-free, non-exclusive license under certain intellectual property owned or controlled by the Company to perform research activities in the Beam Field (the

"Beam Research License"). The Company provided Beam with an exclusive option to obtain a Beam Development and Commercialization License to three additional groups of intellectual property owned or controlled by the Company, on a group by group basis, during the specified option period, subject to certain exceptions. Pursuant to the Beam License Agreement, Beam will use commercially reasonable efforts to develop a product that includes the rights licensed to Beam within a specified period of time and to commercialize any such product that have received regulatory approval in certain specified countries.

As consideration for the license and option rights granted to Beam, the Company received a nominal one-time, non-refundable, non-creditable upfront cash payment. The Company also received non-cash consideration, consisting of a low to mid-single digit million number of shares of Beam Series A-1 and A-2 preferred stock, having an aggregate fair value of approximately $3.6 million. The Company is eligible to receive additional consideration if Beam elects to exercise its option to obtain a Beam Development and Commercialization License to the three categories of intellectual property underlying the Research License, for a fee ranging from a mid-teen million dollar amount to a low to mid-eight digit dollar amount per group, depending on the timing of the option exercise. Additionally, Beam is required to reimburse the Company for certain payments the Company may be obligated to make under the Company's existing license agreements related to the intellectual property being licensed to Beam, including (i) development, regulatory and commercial milestone payments and certain sublicense income payments due as a result of the Beam License Agreement and (ii) a percentage of the annual maintenance fees and patent fees due to certain of the Company's licensors. In addition, to the extent any products are commercialized under a Beam Development and Commercialization License, the Company would be entitled to receive royalty payments equivalent to the royalties that would be due from the Company to any applicable licensors of the Company related to the sales of such licensed products, plus an additional low single-digit percentage royalty. Additionally, if Beam exercises its right to obtain a Beam Development and Commercialization License to one of the categories of optioned intellectual property comprising Company-owned intellectual property and any related licensed products that are commercialized, the Company would be entitled to tiered low single-digit royalty payments related to sales of such licensed products.

The license rights and option rights granted to Beam are subject to the terms and conditions of the underlying license agreements that the Company is a party to and under which the Company licensed rights or option rights to Beam and the termination of such in-licenses, as applicable. Unless earlier terminated by either party pursuant to the terms of the agreement, the Beam License Agreement will continue in full force and effect and will expire on a licensed product-by-licensed product and country-by-country basis upon the expiration of the royalty term with respect to such licensed product in such country. Beam has the right, at its sole discretion, at any time to terminate the Beam License Agreement in its entirety or on a group-by-group of intellectual property basis, upon ninety days written notice to the Company. Upon termination of the Beam License Agreement, all rights and licenses granted by the Company to Beam (including the rights to exercise options and obtain such licenses) will immediately terminate and patents within a group of patents will no longer be deemed licensed patents. Expiration or termination of the Beam License Agreement for any reason does not release either party of any obligation or liability which had accrued or which is attributable to a period prior to such expiration or termination.

Accounting Analysis

The Company has identified the following performance obligations (i) the Beam Development and Commercialization License and (ii) the Beam Research License. In addition, the Company has concluded the option to obtain additional Beam Development and Commercialization Licenses to up to three additional groups of patents in the future is considered a marketing offer as the options did not provide any discounts or other rights that would be considered a material right in the arrangement.

As of December 31, 2018, the total transaction price at the inception of the arrangement was determined to be approximately $3.8 million, consisting of the upfront cash payment and non-cash consideration related to the shares of Beam preferred stock. The Company determined the fair value based on the price paid by other unrelated investors for such shares. The consideration associated with the exercise of the option(s) will be accounted for if and when Beam elects to purchase the additional licenses. The other forms of consideration, including the development and regulatory milestone reimbursement, the sublicense income reimbursement, the maintenance fee reimbursement and the patent costs reimbursement were estimated based on the most-likely amount and were excluded from the initial transaction price as the

most-likely amount was estimated to be zero or the amount was otherwise fully constrained due to the significant uncertainties surrounding such payments. The commercial-based milestone reimbursement and the sales-based royalty payments will be recognized when the related sales occur as they were determined to relate predominantly to the licenses granted and therefore have also been excluded from the transaction price.

The total transaction price at the inception of the arrangement was allocated to the performance obligations in the aggregate, as the Beam Development and Commercialization License and the Beam Research License were delivered simultaneously with one another, at inception of the arrangement, when the licenses were made available for Beam's use and benefit. Accordingly, the satisfaction of each performance obligation occurs at inception of the arrangement and the transaction price at the inception of the arrangement is recognized in its entirety at such time. The Company will re-evaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur. There were no changes to the transaction price during the year ended December 31, 2018.

During the year ended December 31, 2018, the Company recognized revenue under the Beam License Agreement of approximately $4.0 million. The revenue is classified as collaboration and other research and development revenues in the accompanying consolidated statement of operations and the Beam preferred stock is classified in restricted cash and other non-current assets.

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 following is a summary of such in-license agreements that are significant to the Company's business.

Cas9-I License Agreement

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 and the Company and Broad 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 $750.0 million to $10.0 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 more fully 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, as described more fully in 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 License 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.

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-I License Agreement or the Cas9-II 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 under the Cas9-II License Agreement during the fourth quarter of 2017 when the Company's market capitalization reached $1.0 billion, which the Company settled in January 2018, as more fully described in 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, 2018, 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, 2018:

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,	
	2018	2017
Shares reserved for outstanding stock option awards under the 2013 Stock Incentive Plan, as amended	873,373	1,220,567
Shares reserved for outstanding stock option awards under the 2015 Stock Incentive Plan	3,709,225	2,921,987
Shares reserved for outstanding inducement stock option award	107,188	225,000
Remaining shares reserved, but unissued, for future awards under the 2015 Stock Incentive Plan	3,233,031	2,502,338
Remaining shares reserved, but unissued, for future awards under the 2015 Employee Stock Purchase Plan	1,175,224	751,242
	9,098,041	7,621,134

March 2018 Common Stock Sales Agreement

In March 2018, 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 ("2018 ATM Program") for aggregate sales proceeds of $150.0 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 Securities and Exchange Commission ("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. In November 2018, the Company sold an aggregate of 1,107,000 shares of its common stock under the 2018 ATM Program at an average price of $26.95 per share for net proceeds of $28.4 million.

12. Stock-Based Compensation

2013 Stock Incentive Plan

In September 2013, the board of directors adopted the 2013 Stock Incentive Plan, which was subsequently amended (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. In January 2019, the shares under the 2015 Plan were increased by 1,961,156 shares pursuant to the annual increase described in the prior sentence.

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. In January 2019, the shares under the 2015 ESPP Plan were increased by 490,289 shares pursuant to the annual increase described in the prior sentence.

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,		
	2018	2017	2016
Research and development	$ 14,734	$ 15,131	$ 12,647
General and administrative	11,864	8,233	4,234
Total stock-compensation expense	$ 26,598	$ 23,364	$ 16,881

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 as the restricted stock

vests. A summary of the status of and changes in unvested restricted stock as of December 31, 2017 and 2018 is as follows:

	Shares	Weighted Average Grant Date Fair Value Per Share
Unvested Restricted Common Stock as of December 31, 2017	513,225	$ 18.70
Issued	—	—
Vested	(243,225)	$ 8.32
Forfeited	—	—
Unvested Restricted Common Stock as of December 31, 2018	270,000	$ 28.05

The expense related to restricted stock awards granted to employees and non-employees was $0 million and $2.4 million, respectively, for the year ended December 31, 2018. 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.

As of December 31, 2018, the Company had no unrecognized stock-based compensation expense related to its employee unvested restricted stock awards and $6.0 million in unrecognized stock-based compensation expense related to its non-employee unvested restricted stock awards which is expected to be recognized over a remaining weighted average vesting period of 3.7 years.

Stock Options

Certain of the Company's stock option agreements allowed 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 were subject to repurchase by the Company if the employees ceased to provide service to the Company, with or without cause. As such, the Company did not treat the exercise of unvested options as a substantive exercise. The Company 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 was reclassified into stockholders' equity as the shares vested. As of June 30, 2018, the early exercise stock options were fully vested.

The following is a summary of stock option activity for the year ended December 31, 2018:

	Shares	Weighted Average Exercise Price	Remaining Contractual Life	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2017	4,372,136	$ 17.28	8.5	$ 60,591
Granted	1,884,411	$ 35.29	—	—
Exercised	(752,674)	$ 13.78	—	—
Cancelled	(814,087)	$ 24.88	—	—
Outstanding at December 31, 2018	4,689,786	$ 23.80	7.9	$ 20,686
Exercisable at December 31, 2018	2,061,769	$ 18.34	7.0	$ 15,222

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. The Company had no unvested restricted common stock outstanding at December 31, 2018 and had 4,572 shares of unvested restricted common stock outstanding at December 31, 2017, resulting from the exercise of unvested stock options.

The total intrinsic value of options exercised for the years ended December 31, 2018, 2017 and 2016 was $15.9 million, $5.0 million and $0.9 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, 2018, 2017, and 2016 was $24.91, $16.07 and $14.10, respectively. The expense related to options granted to employees and directors was $19.9 million, $12.3 million and $6.0 million for the years ended December 31, 2018, 2017, and 2016, 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,		
	2018	2017	2016
Expected volatility	77.5 %	77.8 %	78.4 %
Expected term (in years)	6.25	6.25	6.25
Risk free interest rate	2.9 %	2.1 %	1.5 %
Expected dividend yield	—	—	—

There were no options granted to persons other than employees and directors during the year ended December 31, 2018. For the years ended December 31, 2018, 2017 and 2016, 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,		
	2018	2017	2016
Expected volatility	—	—	76.5 %
Expected term (in years)	—	—	10.0
Risk free interest rate	—	—	1.6 %
Expected dividend yield	—	—	—

As of December 31, 2018, the Company had unrecognized stock-based compensation expense related to its employee stock options of $47.4 million which the Company expects to recognize over a remaining weighted average vesting period of 2.45 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 $0.7 million and $0.5 million in contributions to the 401(k) Plan for the years ended December 31, 2018 and 2017, respectively.

14. Income Taxes

The Company had no income tax expense due to operating losses incurred for the years ended December 31, 2018, 2017 and 2016.

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,		
	2018	2017	2016
Income tax computed at federal statutory tax rate	21.0 %	34.0 %	34.0 %
State taxes, net of federal benefit	6.4 %	5.9 %	3.5 %
General business credit carryovers	4.4 %	2.5 %	1.5 %
Non-deductible expenses	0.6 %	(2.1)%	(3.6)%
Federal tax rate reduction	— %	(24.7)%	— %
Change in valuation allowance	(32.4)%	(15.6)%	(35.4)%
	— %	— %	— %

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. The Company does not currently have any foreign subsidiaries and the international aspects of the Tax Act are not applicable.

In December 2017, the SEC staff issued Staff Accounting Bulletin No. 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. As of December 31, 2018, the Company had completed its accounting for all of the tax effects of the enactment of the Tax Act; including the effects on its existing deferred tax balances. The Company has not recognized any material adjustment to the provisional estimate that was previously recorded related to the Tax Act.

The principal components of the Company's deferred tax assets and liabilities consist of the following at December 31, 2018 and 2017 (in thousands):

	Year Ended December 31,	
	2018	2017
Deferred tax assets:		
Net operating loss carryforwards	$ 20,302	$ 27,726
Tax credit carryforwards	10,059	5,259
Accrued expenses	3,099	2,079
Capitalized patent costs	33,101	26,307
Deferred revenue	34,039	7,151
Construction financing lease obligation	9,100	9,352
Other	8,347	4,978
Total deferred tax assets	118,047	82,852
Less valuation allowance	(109,091)	(73,301)
Net deferred tax assets	8,956	9,551
Deferred tax liabilities—depreciation and amortization	(8,956)	(9,551)
Net deferred taxes	$ —	$ —

The Company has incurred net operating losses ("NOL") since inception. At December 31, 2018 and 2017, the Company had federal and state net operating loss carryforwards of $147.8 million and $202.7 million, respectively, which expire beginning in 2035 and will continue to expire through 2037. As of December 31, 2018 and 2017, the

Company had federal and state research and development tax credits carryforwards of $10.8 million and $5.6 million, respectively, which expire beginning in 2028 and will continue to expire through 2038.

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 conducted an analysis under Section 382 to determine if historical changes in ownership through December 31, 2017 would limit or otherwise restrict its ability to utilize its NOL and research and development credit carryforwards. As a result of this analysis, the Company does not believe there are any significant limitations on its ability to utilize these carryforwards. However, future changes in ownership occurring after December 31, 2017 could affect the limitation in future years, and any limitation may result in expiration of a portion of the NOL or research and development credit carryforwards before utilization.

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. The Company’s 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 $109.1 million and $73.3 million has been established at December 31, 2018 and 2017, respectively. The increase in the valuation allowance of $35.8 million for the year ended December 31, 2018 was primarily due to current period pre-tax losses incurred and research tax credits generated.

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, 2018 and 2017, 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. The Company will file an initial Colorado tax return for 2018. 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, 2018. 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 shares of common stock 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 shares of common stock 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 closing of the November 2018 ATM Offering, the January 2018 ATM Offering, the 2017 December Offering and the 2017 March Offering, the Company sold 1,107,000 shares, 1,429,205 shares, 2,265,500 shares and 4,600,000 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 years ended December 31, 2018 and 2017 and is expected to continue to impact the year-over-year comparability of the Company's net loss per share calculations for the next 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,	
	2018	2017
Unvested restricted common stock	270,000	513,225
Outstanding stock options	4,689,786	4,372,126
Estimated number of shares issuable for convertible notes [1]	—	244,896
Total	4,959,786	5,130,247

(1) Represents the number of shares of common stock 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 common 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 year ended December 31, 2016, the Company paid a related party $1.4 million in rent and facility-related fees. The Company did not make any payments to this related party during the years ended December 31, 2018 or 2017. The Company received $0.4 million and $0.8 million in rent and facility-related fees from a related party during the years ended December 31, 2018 and 2017, respectively, in connection with subleasing a portion of its headquarters; no rent or facility-related payments were received from this related party during the year ended December 31, 2016. During the years ended December 31, 2018 and 2017, the Company paid a related party $0.8 million and $0.3 million, respectively, in connection with certain research and development expenses. The Company did not make any payments to this related party during the year ended December 31, 2016.

17. Selected Quarterly Financial Data (unaudited) –

The following table contains selected quarterly financial information from 2018 and 2017. 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, 2018	June 30, 2018	September 30, 2018	December 31, 2018
	(in thousands, except per share data)			
Total collaboration and other research and development revenues	$ 3,927	$ 7,372	$ 14,519	$ 6,119
Total operating expenses	35,486	47,029	30,777	32,372
Total other income (expense), net	620	934	1,020	1,199
Net loss	$ (30,939)	$ (38,723)	$ (15,238)	$ (25,054)
Net loss applicable to common stockholders	$ (30,939)	$ (38,723)	$ (15,238)	$ (25,054)
Net loss per share applicable to common stockholders — basic and diluted	$ (0.67)	$ (0.82)	$ (0.32)	$ (0.52)

	Three Months Ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
	(in thousands, except per share data)			
Total collaboration and other research and development revenues	$ 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)

18. Subsequent Events

In February 2019, the Company entered into a co-development and commercialization agreement with an affiliate of Allergan to memorialize the Profit-Sharing Arrangement with respect to the LCA10 Program.

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 principal executive officer and our principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2018. 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, 2018, our principal executive officer and principal 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, 2018.

The effectiveness of our internal control over financial reporting as of December 31, 2018, has been audited by Ernst & Young LLP, an independent registered public accounting firm, and has issued an attestation report on such audit, which is included herein.

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, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

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

Opinion on Internal Control over Financial Reporting

We have audited Editas Medicine, Inc.'s internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Editas Medicine, Inc. (the "Company") maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of Editas Medicine, Inc. as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, redeemable convertible preferred stock and stockholders' (deficit) equity, and cash flows for each of the three years in the period ended December 31, 2018, and the related notes and our report dated February 28, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 of the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's 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 generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding

prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, 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.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 28, 2019

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 III Directors," "Directors Continuing in Office," "Executive Officers Who Are Not Directors," and "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 2019 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 2019 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 2019 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 2019 Annual Meeting of Stockholders, which information is incorporated herein by reference.

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 2019 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	

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File No.	Date of Filing	Exhibit Number	
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	10.12	
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†	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. (the "Broad")	8-K	001-37687	1/23/2017	99.2	
10.15	Amendment No.1 to Amended and Restated Cas9-I License Agreement, by and among Editas Medicine, Inc., President and Fellows of Harvard College, and Broad, dated March 3, 2017	8-K	001-37687	3/7/2017	99.1	
10.16†	Amended and Restated License and Collaboration Agreement, dated May 3, 2018, between the Registrant and Juno Therapeutics, Inc.	10-Q/A	001-37687	10/23/2018	10.1	
10.17†	Sponsored Research Agreement, dated June 7, 2018, between the Registrant and Broad	10-Q/A	001-37687	10/23/2018	10.2	
10.18+	Summary of Director Compensation Program	S-1	333-208856	1/4/2016	10.24	
10.19+	2015 Employee Stock Purchase Plan	S-1	333-208856	1/4/2016	10.25	
10.20+	Severance Benefits Plan	S-1	333-208856	1/4/2016	10.27	
10.21	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers	S-1	333-208856	1/4/2016	10.28	
10.22	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	
10.23†	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	
10.24†	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	

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File No.	Date of Filing	Exhibit Number	
10.25†	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	
10.26	Common Stock Sales Agreement, dated March 3, 2017, by and between the Registrant and Cowen and Company, LLC ("Cowen")	S-3	333-216444	3/3/2017	1.2	
10.27	Common Stock Sales Agreement, dated March 12, 2018, by and between the Registrant and Cowen	S-3	333-223596	3/12/2019	1.2	
10.28+	Separation Agreement, by and between the Registrant and Gerald Cox, M.D., Ph.D.					X
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: February 28, 2019

By: /s/ Cynthia Collins
Cynthia Collins
Principal 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/ Cynthia Collins Cynthia Collins	Director (principal executive officer)	February 28, 2019
/s/ Andrew A. F. Hack Andrew A.F. Hack, M.D., Ph.D.	Chief Financial Officer (principal financial and accounting officer)	February 28, 2019
/s/ James Mullen James Mullen	Chairman of the Board	February 28, 2019
/s/ Andrew Hirsch Andrew Hirsch	Director	February 28, 2019
/s/ Jessica Hopfield Jessica Hopfield, Ph.D.	Director	February 28, 2019
/s/ David Scadden David Scadden, M.D.	Director	February 28, 2019
/s/ Akshay K. Vaishnaw Akshay K. Vaishnaw, M.D., Ph.D.	Director	February 28, 2019

Exhibit 10.28

11 Hurley Street
Cambridge, MA 02141
P 617-401-9000
F 617-494-0985

August 24, 2018

Gerald Cox
48 Avon Circle
Needham, MA 02494

Dear Gerry,

The purpose of this letter (the "Separation Agreement") is to set forth the terms regarding your separation of employment as Chief Medical Officer from Editas Medicine, Inc. ("Editas" or the "Company"), including certain severance payments and benefits you may elect in exchange for certain other commitments and the general release provided herein:

1. **Employment with the Company.** You are being removed from the position of Chief Medical Officer with the Company effective November 9, 2018, unless terminated at an earlier date by you or the Company (any such date, the "Termination Date"). You acknowledge that from and after November 9, 2018, you shall not have any authority, and shall not represent yourself, as an employee or agent of the Company.

2. **Payments.** You will receive on the Termination Date:

    a. Payment reflecting pay for any time worked through the Termination Date that has not already been paid through the Company's regular payroll process.

3. **Retention Benefit**. If your employment with the Company is not terminated by you or the Company prior to November 9, 2018, and so long as you make yourself available to answer questions and provide advice from November 12, 2018 through December 14, 2018, you will be eligible for the following Retention Benefit:

    a. You will be eligible to receive a bonus for 2018. Any such bonus will be based on your current target bonus (40%) subject to modification based only on Corporate Achievement and will be paid to you at the same time that 2018 bonuses are paid out to existing employees of the Company (the "Retention Payment"). For the avoidance of doubt, such bonus will not be determined or modified based on achievement of your individual goals.

4. **Severance Benefits.** In accordance with and subject to the Company's Severance Benefits Plan (the "Severance Plan"), subject to your execution of this Separation Agreement on or before August 27, 2018 and execution and non-revocation of the Release, attached as **Exhibit A**, within twenty-one (21) days of your last day of employment with the Company, the Company agrees to provide you with the following

severance benefits (collectively, the "Severance Benefits"):

a. **Cash Severance:** The Company will continue to pay you your monthly Base Salary (as defined in the Severance Plan), less all applicable taxes and withholdings, as severance pay for a period of twelve (12) months from the Termination Date. Subject to the Severance Plan, this severance pay will be paid in installments in accordance with the Company's regular payroll practices, but in no event shall payments begin earlier than the Company's first payroll date following the Release Effective Date (as defined in the Severance Plan).

b. **COBRA Contributions:** You will be entitled to the COBRA contributions in accordance with Section 8(a) of the Severance Plan.

Also, regardless of your signing this Separation Agreement, upon the termination of your employment with the Company you may elect to continue your medical and dental insurance, subject to the requirements of COBRA. You will be sent a COBRA qualifying notice under separate cover and subsequent notices as required by applicable law or regulation. Your costs to continue the coverage will be set forth in these notices. The "qualifying event" under COBRA shall be deemed to have occurred on the Termination Date. "COBRA" is the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended.

5. **Extension of Stock Option Exercise Period.** Subject to the approval of the Compensation Committee of the Company's Board of Directors, the Company shall extend to May 9, 2019 the exercise period for all options previously awarded by the Company to you as part of your employment (the "Employee Option Agreements") and that have vested up to and including November 9, 2018, your last day as a Company employee. Following May 9, 2019, your ability to exercise any vested options under your Employee Option Agreements, to the extent not previously exercised, shall terminate. For the avoidance of doubt, vesting under all Employee Option Agreements shall cease effective as of November 9, 2018 and no additional vesting shall occur under such Employee Option Agreements as a result of you being available to answer questions and provide advice between November 12 and December 14, 2018.

6. **Unemployment Compensation**. You may seek unemployment benefits as a result of the termination of your employment with the Company. Decisions regarding eligibility for and amounts of unemployment benefits are made by the applicable state unemployment agency, not by Editas. Editas agrees to provide any and all requested or necessary documents to enable you to seek unemployment benefits, and further agrees that it will not contest your eligibility for unemployment benefits.

7. **Other Benefits.** You acknowledge that, except as provided in Section 4(b) above, all employee benefits provided to you by the Company will terminate on the Termination Date subject to any conversion or other rights, including rights to vested benefits, that you may have under any such benefit plans, including, without limitation, the Severance Plan, 2015 Stock Incentive Plan and related Awards and your Inducement

Stock Option Agreement.

8. **No Amounts Owing.** You acknowledge and agree that the Severance Benefits provided in Section 4 of this Separation Agreement are in accordance with the Severance Plan and shall confer no benefit on anyone other than you. You further acknowledge and agree that you have been paid and provided all wages, bonuses, and any other form of compensation that may be currently due to you as of the date you sign this Separation Agreement except for wages due on the next regular payroll date, the Retention Payment and Severance Benefits.

9. **Release of Claims.** In exchange for the Retention Payment and Severance Benefits described in Sections 3 and 4 above, respectively, as well as other good and valuable consideration described herein, you agree to execute a general release and waiver of claims (the "Release") against the Company and each of its present, former, and future parents, affiliates, predecessors in interest, successors in interest, subsidiaries, trustees, officers, directors, employees, agents, representatives, attorneys, insurers, and assigns in the form attached as **Exhibit A**. This Release includes claims of discrimination, including age discrimination, and all other claims relating to your hiring, employment, and termination of employment by the Company.

10. **Scope of Disclosure Restrictions.** Nothing in this Separation Agreement prohibits either you or the Company communicating with government agencies about possible violations of federal, state, or local laws or otherwise providing information to government agencies, filing a complaint with government agencies, or participating in government agency investigations or proceedings. Neither you nor the Company are required to notify the other of any such communications; provided, however, that nothing herein authorizes the disclosure of information either party obtained through a communication that was subject to the attorney-client privilege. Further, notwithstanding your confidentiality and nondisclosure obligations, you are hereby advised as follows pursuant to the Defend Trade Secrets Act: "An individual shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal. An individual who files a lawsuit for retaliation by an employer for reporting a suspected violation of law may disclose the trade secret to the attorney of the individual and use the trade secret information in the court proceeding, if the individual (A) files any document containing the trade secret under seal; and (B) does not disclose the trade secret, except pursuant to court order."

11. **Return of Company Property.** You agree to return all Company property, including but not limited to keys, access cards, computer and electronic equipment, mobile phone, documents, and files to the Company on or before December 14, 2018.

12. **Non-Assignment.** You warrant and represent to the Company that you have not assigned or transferred or attempted to assign or transfer to any person any claim or

matter recited in the Release or any part or portion thereof, and agree to indemnify and hold harmless the Company from and against any claim.

13. **Confidentiality**. You hereby acknowledge and agree that all information relating in any way to the negotiation of this Separation Agreement, including the terms and amount of financial consideration provided for in this Separation Agreement, shall be held confidential and shall not be disclosed to any other persons, business entity or government agency except that you may disclose the terms of this Separation Agreement to immediate family members, tax authorities, attorney, tax/financial advisor, and/or any state unemployment agency, if necessary in connection with any effort by you to collect unemployment benefits, (provided that any individual to whom disclosure is made agrees to be bound by these confidentiality obligations) or as otherwise may be required by law or subpoena. Nothing in the Separation Agreement is intended to interfere with or should be interpreted as interfering with the rights of employees or former employees under Section 7 of the National Labor Relations Act (NLRA).

14. **Non-Disparagement**. You hereby acknowledge and agree that you will not make any statements, whether verbally or in writing, that are professionally or personally disparaging of the Company, or those persons known by you to be or to have been Company officers, directors, employees, agents, or representatives and you further agree not to engage in any conduct that is intended to harm the reputation of the Company or those persons known by you to be or have been Company officers, directors, employees, agents, or representatives. In turn, the Company agrees that we will not make professionally or personally disparaging comments regarding you and will limit reference checks to dates of employment and last position title and level.

15. **Your Continuing Obligations.** You acknowledge that while an employee of Editas you executed an Employee Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreement, a copy of which is attached as **Exhibit B** (the "Restrictive Covenant Agreement"), and that notwithstanding your termination you continue to remain bound by that agreement.

16. **Successors and Assigns.** This Separation Agreement shall be binding upon the respective legal representatives, heirs, and successors of the parties, to the extent permitted by law.

17. **Notices.** Any notices required to be given in connection with this Separation Agreement or Exhibit A shall be given by either by overnight delivery (FED-EX, UPS, or similar over-night carrier) or mailed by certified mail, return receipt requested, postage prepaid, to you at the address above or to the Company as follows: **Semi Trotto, Head of Human Resources, Editas Medicine, 11 Hurley Street, Cambridge, MA 02142.** The address for notices may be changed by providing you or the Company with notice pursuant to this Section 17.

18. **Voluntary Agreement.** By executing this Separation Agreement, you are acknowledging that you have been afforded sufficient time to understand the terms

and effects of this Separation Agreement, that your agreements are made voluntarily, knowingly and without duress, and that neither the Company, nor its agents or representatives, have made any representations inconsistent with the provisions of this Separation Agreement.

19. **Entire Agreement.** You acknowledge that this Separation Agreement, the Severance Plan, 2015 Stock Incentive Plan and related Awards, your Inducement Stock Option Agreement and the Restrictive Covenant Agreement set forth the entire agreement between you and the Company concerning your termination and fully supersedes any and all prior agreements or understandings between you and the Company pertaining to the subject matter hereof. This Separation Agreement may only be modified in a written document signed by you and an authorized representative of the Company. In the event any provision of this Separation Agreement is held invalid, all remaining provisions of the Separation Agreement shall remain in full force and effect.

20. **Severability.** Should any provision of this Separation Agreement be declared or be determined by any court of competent jurisdiction to be illegal or invalid, the validity of the remaining parts, terms or provisions shall not be affected thereby and said illegal or invalid part, term or provision shall be deemed not to be a part of this Separation Agreement.

21. **Governing Law.** This Separation Agreement shall be governed by and interpreted in accordance with the substantive laws of the Commonwealth of Massachusetts, without regard to its conflict of law principles. You agree that any action, demand, claim or counterclaim relating to the terms and provisions of this Separation Agreement, or its formation or breach, shall be commenced in the Commonwealth of Massachusetts in a court of competent jurisdiction, and you further acknowledge that venue for such actions shall lie exclusively in Massachusetts.

22. **Representations.** The Company has advised you to consult with an attorney of your choosing, concerning this Separation Agreement and Release. You affirm that you have carefully read and fully understand this Separation Agreement and attached Exhibit A and are voluntarily entering this Separation Agreement.

23. **Execution.** This Separation Agreement may be executed in one or more counterparts, each of which when so executed shall be deemed to be an original, and all such counterparts together shall constitute but one and the same instrument. Your signature below reflects your understanding of, and agreement to, the terms and conditions set forth above.

Sincerely,

/s/ Katrine Bosley
By: Katrine Bosley
Title: Chief Executive Officer
Editas Medicine

Attachments

Agreed and accepted this 27th day of August, 2018:

/s/ Gerald Cox
Gerald Cox

EXHIBIT A

GENERAL RELEASE AND WAIVER OF CLAIMS
(INCLUDING AGE DISCRIMINATION IN EMPLOYMENT CLAIMS)

In consideration of the Retention Payment and Severance Benefits set forth in the **August 24, 2018** letter of agreement (the "Separation Agreement") (to which this General Release and Waiver of Claims is attached), I, Gerald Cox, on behalf of my heirs, administrators, executors, representatives, attorneys, agents, insurers, and assigns (collectively, the "Releasors") except as provided below, hereby fully, finally, irrevocably, unconditionally, and voluntarily release and forever discharge Editas Medicine, Inc. ("the Company") and each of its present, former, and future parents, affiliates, predecessors in interest, successors in interest, subsidiaries, trustees, officers, directors, employees, agents, representatives, attorneys, insurers, and assigns (collectively, the "Releasees"), jointly and individually, from any and all claims, suits, charges, complaints, contracts, covenants, promises, debts, losses, sums of money, obligations, demands, judgments, or causes of action of any kind whatsoever, which the Releasors ever had, or now have, or hereafter can, shall or may have, from the beginning of the world to the date of the execution of this Release, whether known or unknown, in law or equity, in tort, contract, by statute, at common law, or on any other basis, whether federal, state, local, or otherwise, including but not limited to claims arising out of or in any way related to my employment by the Company including my hiring, or the termination of that employment, or any related matters, including but not limited to:

(i.) Claims under any federal, state or local laws, regulations, public policy or other requirements relating to the claims or rights of employees, including but not limited to, the Massachusetts Fair Employment Practices Act (Massachusetts General Laws, Chapter 151B), the Massachusetts Payment of Wages Act (Massachusetts General Laws, Chapter 149, Section 148 et seq.), Title VII of the Civil Rights Act of 1964, the Age Discrimination in Employment Act, the Older Workers Benefit Protection Act, the Employee Retirement Income Security Act of 1974, the Equal Pay Act of 1963, the Americans with Disabilities Act, the Family and Medical Leave Act, and the Occupational Health and Safety Act of 1970, all as they may have been amended;

(ii.) Any and all Claims and suits in tort, contract, or wrongful discharge, discrimination, retaliation, or harassment;

(iii.) Any and all Claims arising under common law, including but not limited to any claim for negligent or intentional infliction of emotional distress, promissory estoppel, whistleblower retaliation, fraud, misrepresentation, defamation, negligence, retaliation or violation of public policy;

(iv.) Any and all claims for breach of express or implied contract; and

(v.) Any other Claim that I now have, may have, or have ever had against Releasees based on any conduct up to and including the date of his execution of this Release.

The recitation of specific claims herein is without prejudice to the general release contained herein and is not intended to limit the scope of the general release. This release will remain in effect notwithstanding the discovery or existence of any additional fact or facts different from those which you now know or believe to be true relating to the foregoing released Claims.

Notwithstanding anything to the contrary contained herein, nothing contained in this General Release and Waiver of Claims shall be construed to bar any (a) non-termination related claims under the Massachusetts Workers Compensation Act (M.G.L. c. 152) or any disability insurance policy/plan; (b) rights to vested benefits under any applicable retirement and/or pension and/or deferred compensation plans, including, without limitation the Severance Plan, 2015 Stock Incentive Plan and related Awards, and my Inducement Stock Option Agreement; (c) non-termination related claims under the Employee Retirement Income Security Act (29 U.S.C. § 1001 et seq.); (d) rights under the Consolidated Omnibus Budget Reconciliation Act of 1985 ("COBRA"); (e) claims for unemployment compensation; (f) rights to defense, indemnification and contribution from the Company or its insurers for actions taken by me in the course and scope of my employment with the Company and its parents, subsidiaries and/or affiliates, pursuant to any Company policy and/or governing documents such as its by-laws or any applicable insurance policy, or at common law; (g) claims, actions, or rights arising under or to enforce the terms of the Separation Agreement; (h) any claims arising solely after the execution of this Release; (i) claims for reimbursement of approved business expenses incurred prior to the Termination Date (as defined in the Separation Agreement); or (j) any rights or claims I may have as a shareholder of the Company or holder of options to purchase stock of the Company.

I acknowledge that I have been advised to consult with an attorney, and affirm that I have done so, before signing this Release, particularly the release of ADEA claims. I acknowledge that the Company has given me twenty-one days to consider signing this Release. I also acknowledge that, in signing this Release, I am not relying on any other statements or explanations made by the Company.

This Release will become effective seven (7) days after it is signed. I understand that I may revoke this Release within seven (7) days after it is signed by giving written notice by overnight delivery (FED-EX, UPS, or similar over-night carrier) or mailed by certified mail, return receipt requested, postage prepaid to the Company as follows: Semi Trotto, Head of Human Resources, Editas Medicine, 11 Hurley Street, Cambridge, MA 02142, and that it shall not become effective until the expiration of the seven-day revocation period. If I choose to revoke the Release, I understand that the Separation Agreement, of which this Release is an essential part, will become null and void and that the Company will not owe me the Retention Payment or Severance Benefits set forth in the Separation Agreement.

In witness whereof, I, Gerald Cox, have caused this General Release and Waiver of Claims to be executed and sealed this _____ day of _____, 2018.

_____
Gerald Cox

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statements (Form S-3 No. 333-216528, 333-222266, and 333-223596) of Editas Medicine, Inc.,

(2) Registration Statement (Form S-8 No. 333-209351) pertaining to the Editas Medicine, Inc. 2013 Stock Incentive Plan, 2015 Stock Incentive Plan and 2015 Employee Stock Purchase Plan,

(3) Registration Statement (Form S-8 No. 333-214556) pertaining to the Editas Medicine, Inc. Inducement Stock Option Award, and

(4) Registration Statements (Form S-8 Nos. 333-216445 and 333-223529) pertaining to the 2015 Stock Incentive Plan and 2015 Employee Stock Purchase Plan;

of our reports dated February 28, 2019, with respect to the consolidated financial statements of Editas Medicine, Inc. and the effectiveness of internal control over financial reporting of Editas Medicine, Inc., included in this Annual Report (Form 10-K) of Editas Medicine, Inc. for the year ended December 31, 2018.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 28, 2019

Exhibit 31.1

CERTIFICATIONS

I, Cynthia Collins, 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: February 28, 2019

By: /s/ Cynthia Collins
Cynthia Collins
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: February 28, 2019

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 PEO 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, 2018, 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: February 28, 2019

By: /s/ Cynthia Collins
Cynthia Collins
Principal Executive Officer

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