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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2017

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 001-37923

CRISPR THERAPEUTICS AG

(Exact name of Registrant as specified in its Charter)

Switzerland **(State or other jurisdiction of incorporation or organization)**	**Not Applicable** **(I.R.S. Employer Identification No.)**
Baarerstrasse 14 **6300 Zug, Switzerland** **(Address of principal executive offices)**	**Not Applicable** **(Zip Code)**

Registrant's telephone number, including area code: +41 (0)41 561 32 77

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

Title of each class	Name of each exchange on which registered
Common shares, nominal value CHF 0.03 per share	The Nasdaq Global Market

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

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

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

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

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

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

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

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

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

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

As of June 30, 2017, the aggregate market value of the Common Stock held by non-affiliates of the registrant was approximately $605.5 million, based on the closing price of the registrant's common stock on June 30, 2017.

As of February 28, 2018, 46,976,000 common shares were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement relating to the Annual General Meeting of Shareholders for the year ended December 31, 2017, which the registrant intends to file with the Securities and Exchange Commission pursuant to Regulation 14A within 120 days after the end of the registrant's fiscal year ended December 31, 2017, are incorporated by reference into Part III of this Report.

Table of Contents

Throughout this Annual Report on Form 10-K, the "Company," "CRISPR," "CRISPR Therapeutics," "we," "us," and "our," except where the context requires otherwise, refer to CRISPR Therapeutics AG and its consolidated subsidiaries, and "our board of directors" refers to the board of directors of CRISPR Therapeutics AG.

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," "intend," "expect," "may," "estimate," "predict," "project," "potential" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. 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.

BUSINESS

Overview

We are a leading gene editing company focused on the development of CRISPR/Cas9-based therapeutics. CRISPR/Cas9 stands for Clustered, Regularly Interspaced Short Palindromic Repeats (CRISPR) Associated protein-9 and is a revolutionary technology for gene editing, the process of precisely altering specific sequences of genomic DNA. We are applying this technology to potentially treat a broad set of both rare and common diseases by disrupting, correcting or regulating disease-related genes. We believe that our scientific expertise, together with our gene editing approach, may enable an entirely new class of highly effective and potentially curative treatments for patients for whom current biopharmaceutical approaches have had limited success. Our most advanced programs target beta-thalassemia and sickle cell disease, two hemoglobinopathies that have high unmet medical need.

The use of CRISPR/Cas9 for gene editing was derived from a naturally occurring viral defense mechanism in bacteria and has been described by leading scientific journals as a breakthrough technology. The application of CRISPR/Cas9 for gene editing was co-invented by one of our scientific founders, Dr. Emmanuelle Charpentier, a director of the Max-Planck Institute for Infection Biology in Berlin. Dr. Charpentier and her collaborators published work elucidating the mechanism by which the Cas9 endonuclease, a key component of CRISPR/Cas9, can be programmed to cut double-stranded DNA at specific locations. We have acquired rights to the foundational intellectual property encompassing CRISPR/Cas9 and related technologies from Dr. Charpentier, and continue to strengthen our intellectual property estate through our own research and additional in-licensing efforts, furthering our leadership in the development of CRISPR/Cas9-based therapeutics.

Our product development and partnership strategies are designed to exploit the full potential of the CRISPR/Cas9 platform while maximizing the probability of successfully developing our product candidates. We are pursuing a two-pronged product development strategy using both *ex vivo* and *in vivo* approaches. Our most advanced product candidate, referred to as CTX001, targets sickle cell disease and beta-thalassemia with an *ex vivo* approach whereby cells are harvested from a patient, treated with a CRISPR/Cas9-based therapeutic and reintroduced into the patient. In December 2017, we filed clinical trial applications (CTAs) for CTX001 in major European countries for beta-thalassemia and plan to initiate clinical trials during 2018. We have chosen to conduct our lead programs in these two hemoglobinopathies given the relative ease of editing genes *ex vivo*, the significant unmet medical need associated with sickle cell disease and beta-thalassemia, and the well-understood genetics of these diseases. Drawing from the *ex vivo* gene editing expertise gained through our lead programs, we are advancing immuno-oncology cell therapy programs starting with CTX101, a healthy donor-derived gene-edited allogeneic CAR-T therapy targeting CD19-positive malignancies. In addition, we have two earlier stage allogeneic CAR-T programs targeting B-Cell maturation antigen, or BCMA and CD70. Beyond our *ex vivo* programs, we are also pursuing select *in vivo* applications, whereby the CRISPR/Cas9-based therapeutic is delivered directly to target cells within the human body. Our initial *in vivo* applications will leverage well-established delivery technologies for gene-based therapeutics.

Given the numerous potential therapeutic applications for CRISPR/Cas9, we have partnered strategically to broaden the indications we can pursue and accelerate development of programs by accessing specific technologies and/or disease-area expertise. In particular, we established a joint venture, called Casebia Therapeutics LLP, with Bayer HeathCare and its subsidiaries, or Bayer, in which we have a 50% interest, and a collaboration agreement with Vertex Pharmaceuticals Incorporated, or Vertex, in order to pursue specific indications where these companies have outstanding and distinctive capabilities. In December 2017, we entered into a joint development and commercialization agreement with Vertex to co-develop and co-commercialize CTX001 as part of our existing collaboration. The significant resource commitments by our partners underscore the potential of our platform, as well as their dedication to developing transformative CRISPR/Cas9-based therapeutics.

Our mission is to create transformative gene-based medicines for serious human diseases. We believe that our highly experienced team, together with our scientific expertise, product development strategy, partnerships and intellectual property position us as a leader in the development of CRISPR/Cas9-based therapeutics.

Gene Editing Background

There are thousands of diseases caused by aberrant DNA sequences. Traditional small molecule and biologic therapies have had limited success in treating many of these diseases because they fail to address the underlying genetic causes. Newer approaches such as RNA therapeutics and viral gene therapy more directly target the genes related to disease, but each has clear limitations. RNA-based therapies, such as mRNA and siRNA, face challenges with repeat dosing and related toxicities. Non-integrating viral gene therapy platforms, such as adeno-associated virus, or AAV, may have limited durability because they do not permanently change the genome and have limited efficacy upon re-administration due to resulting immune responses. Integrating viral gene therapy platforms, such as lentivirus, permanently alter the genome but do so randomly, which leads to the potential for undesirable mutations. Additionally, cells may recognize the transduced genes as foreign and respond by reducing their expression, limiting their efficacy. Thus, while our understanding of genetic diseases has increased tremendously since the mapping of the human genome, our ability to treat them effectively has been limited.

We believe gene editing has the potential to enable a next generation of therapeutics and provide curative solutions to many genetic diseases through precise gene modification. The process of gene editing involves precisely altering DNA sequences within the genomes of cells using enzymes to cut the DNA at specific locations. After a cut is made, natural cellular processes repair the DNA to either silence or correct undesirable sequences, potentially reversing their negative effects. Importantly, because the genome itself is modified in this process, the change is permanent in the patient.

Earlier generations of gene-editing technologies, such as zinc finger nucleases (ZFNs), transcription-activator like effector nucleases (TALENs) and meganucleases, rely on engineered protein-DNA interactions. While these systems were an important first step to demonstrate the potential of gene editing, their development has been challenging in practice due to the complexity of engineering protein-DNA interactions. In contrast, CRISPR/Cas9 is guided by RNA-DNA interactions, which are more predictable and straightforward to engineer and apply.

The CRISPR/Cas9 Technology

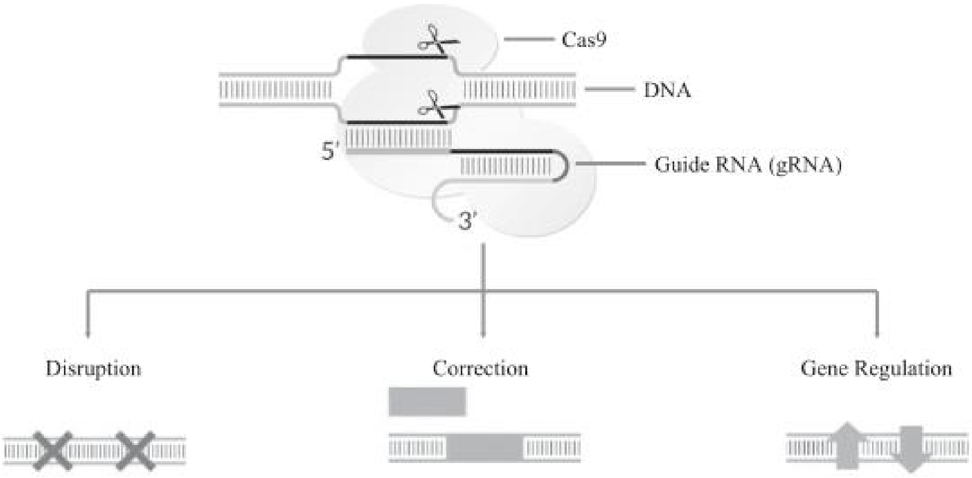
CRISPR/Cas9 evolved as a naturally occurring defense mechanism that protects bacteria against viral infections. Dr. Emmanuelle Charpentier and her collaborators elucidated this mechanism and developed ways to adapt and simplify it for use in gene editing. The CRISPR/Cas9 technology they described consists of three basic components: CRISPR-Associated protein 9, or Cas9, CRISPR RNA, or crRNA, and trans-activating CRISPR RNA, or tracrRNA. Cas9, in combination with these two RNA molecules, is described as “molecular scissors” that can make specific cuts and edits in selected double-stranded DNA.

Dr. Emmanuelle Charpentier and her collaborators further simplified the system for use in gene editing by combining the crRNA and tracrRNA into a single RNA molecule called a guide RNA. The guide RNA binds to Cas9 and can be programmed to direct the Cas9 enzyme to a specific DNA sequence based on Watson-Crick base pairing rules. The CRISPR/Cas9 technology can be used to make cuts in DNA at specific sites of targeted genes, providing a powerful tool for developing gene editing based therapeutics.

Once the DNA is cut, the cell uses naturally occurring DNA repair mechanisms to rejoin the cut ends. If a new DNA template with the correct sequence has been delivered to the cell prior to the time the DNA is cut, it will be incorporated, leading to a correction of the targeted gene, which we refer to as gene correction. Alternatively, if no DNA template is present, the cell will rejoin the two cut ends in a way that will likely lead to the disruption and inactivation of the gene, which we refer to as gene disruption.

CRISPR/Cas9 can also be adapted to regulate the activity of an existing gene without modifying the actual DNA sequence, which we refer to as gene regulation. This is accomplished using a catalytically inactive form of the Cas9 enzyme that can be directed to bind specific DNA sequences without cutting. By linking this inactive Cas9 to proteins that regulate gene function, the activity of specific genes can be either up or downregulated.

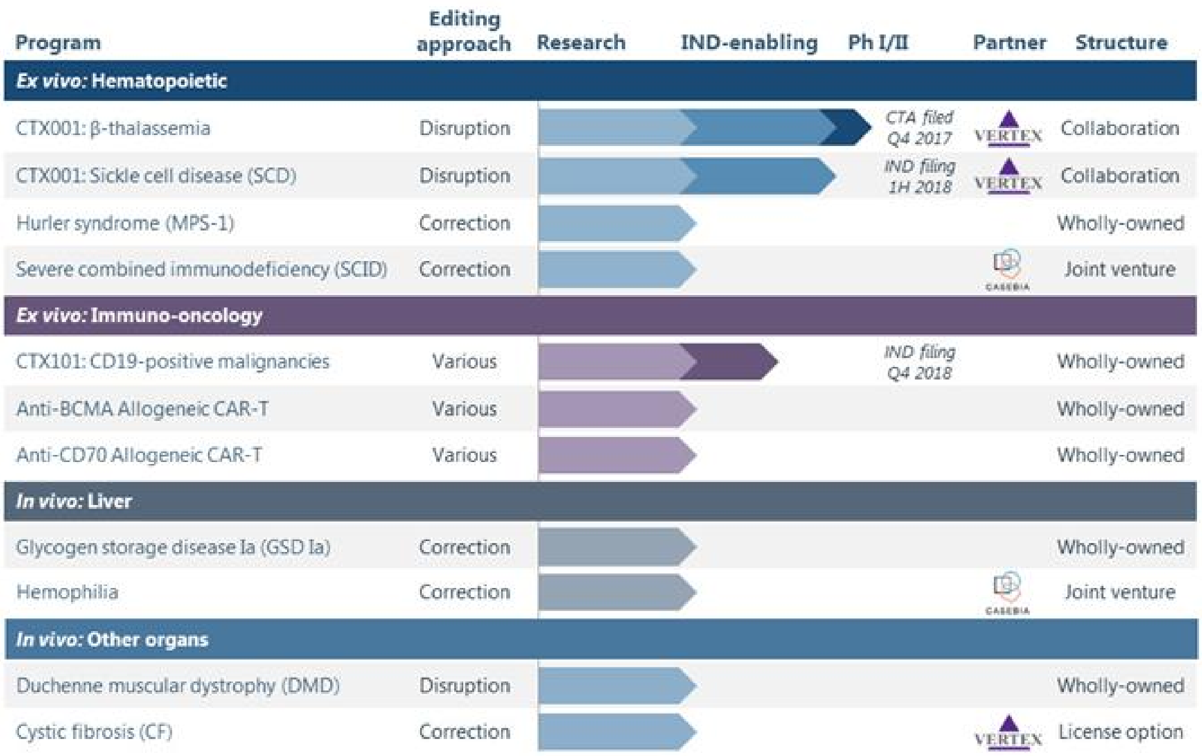
CRISPR/Cas9 gene editing



We believe that CRISPR/Cas9 is a versatile technology that can be used to either disrupt, correct or regulate genes. We intend to take advantage of the versatility and modularity of the CRISPR/Cas9 system to adapt and rapidly customize individual components for specific disease applications. Consequently, we believe that CRISPR/Cas9 may form the basis of a new class of therapeutics with the potential to treat both rare and common diseases.

Our Pipeline

The following table summarizes the status of our product development pipeline:



Ex Vivo *Hematopoietic Programs*

Background

We are primarily utilizing *ex vivo* approaches to treat diseases related to the hematopoietic system, which is the system of organs and tissues, such as bone marrow, the spleen and lymph nodes, involved in the production of blood. Today, many of the hematopoietic system diseases we are targeting are treated with allogeneic hematopoietic stem cell transplants, or allo-HSCT. In performing allo-HSCT, physicians replace a patient's blood-forming cells that contain the defective gene with cells obtained from a different person that contain the normal gene. Unfortunately, not all patients are able to be matched with suitable donors. Patients who do undergo allo-HSCT face a high risk of complications such as infections related to immunosuppression, transplant rejection and graft-versus-host disease, where immune cells in the transplanted tissue (the graft) recognize the recipient (the host) as "foreign" and begin to attack the host's cells.

In contrast to allo-HSCT, our approach harvests stem cells directly from the patient, edits the defective gene *ex vivo*, and reintroduces those same cells back into the patient. We believe this *ex vivo* gene editing approach, which uses the patient's own cells, may provide better results than allo-HSCT.

Our Lead Programs—Hemoglobinopathies

Hemoglobinopathies are a diverse group of inherited blood disorders that result from variations in the synthesis or structure of hemoglobin. Our lead programs in hemoglobinopathies, for which we have partnered with Vertex, aim to develop a single, potentially transformative CRISPR/Cas9-based therapy to treat both beta-thalassemia and sickle cell disease, or SCD. These diseases are caused by mutations in the gene encoding the beta globin protein. Beta globin is an essential component of hemoglobin, a protein in red blood cells that delivers oxygen and removes carbon dioxide throughout the body. Several factors make these attractive lead indications, including: (i) high unmet medical need, (ii) compelling market potential, (iii) well-understood genetics and (iv) the ability to employ an *ex vivo* gene disruption strategy.

Beta-thalassemia

Overview

Beta-thalassemia is a blood disorder that is associated with a reduction in the production of hemoglobin. This disease is caused by mutations that give rise to the insufficient expression of the beta globin protein, which can lead to symptoms related not only to the lack of hemoglobin, but also to the buildup of unpaired alpha globin proteins in red blood cells. The severity of symptoms associated with beta-thalassemia varies depending on the levels of functional beta globin present in the blood cells. The unpaired alpha globin chains are toxic to red blood cells and reduce red blood cell lifespan. In the most severe cases, described as beta-thalassemia major, functional beta globin is either completely absent or reduced, resulting in severe anemia. In these patients, the bone marrow cannot keep pace with the destruction of red blood cells, and thus these patients require periodic blood transfusions. While chronic blood transfusions can be effective at addressing symptoms, they often lead to iron overload, progressive heart and liver failure, and eventually death. Patients with mild forms of beta-thalassemia may experience some mild anemia or even be asymptomatic. The total worldwide incidence of beta-thalassemia is estimated to be 60,000 births annually, the total prevalence in the United States and the European Union is estimated to be approximately 19,000 and there are over 200,000 people worldwide who are alive and registered as receiving treatment for the disease.

Limitations of current treatment options

The most common treatment for beta-thalassemia is chronic blood transfusions. Patients typically receive transfusions every two to four weeks and chronic administration of blood often leads to elevated levels of iron in the body and can cause organ damage over a relatively short period of time. Patients are often given iron chelators, or medicines to reduce iron levels in the blood, which are associated with their own significant toxicities. Low adherence to this burdensome regime often results in death by 30 years of age for patients with transfusion-dependent beta-thalassemia. The only potentially curative therapy for this disease is allo-HSCT, but few patients elect to have this procedure given its associated morbidity and mortality. In developing countries, where chronic transfusions are not available, most patients die in early childhood. We believe that our therapeutic approach could offer a potentially curative treatment for this devastating disease.

Sickle Cell Disease

Overview

SCD is an inherited disorder of red blood cells resulting from a specific mutation in the beta globin gene that causes abnormal red blood cell function. Under conditions of low oxygen concentration, the abnormal hemoglobin proteins aggregate within the red blood cells causing them to become sickled in shape and inflexible. These sickled cells obstruct blood vessels, restricting blood flow to organs, ultimately resulting in anemia, severe pain, infections, stroke, overall poor quality of life and early death.

The worldwide incidence of SCD is estimated to be 300,000 births annually and there are 20 - 25 million people worldwide with the disease. In the United States, the total prevalence is estimated to be 100,000 individuals.

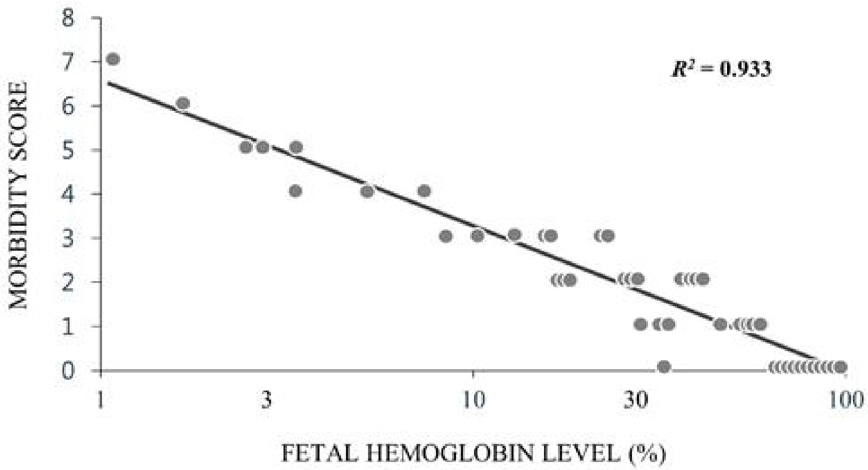
Limitations of current treatment options

As with beta-thalassemia, in regions where access to modern medical care is available, standard treatment for SCD involves chronic blood transfusions, which has the same associated risks of iron overload and toxicities associated with chelation therapy. Allo-HSCT is a second potential treatment option. While allo-HSCT provides the only potentially curative therapeutic path for SCD, it is often avoided given the significant risk of transplant-related morbidity and mortality in these patients.

Our Gene Editing Approach

Our therapeutic approach to treating beta-thalassemia and SCD employs gene editing to upregulate the expression of the gamma globin protein, a hemoglobin subunit that is commonly present only in newborn infants. Hemoglobin that contains gamma globin instead of beta globin protein is referred to as fetal hemoglobin, or HbF. In most individuals HbF disappears in infancy as gamma globin is replaced by beta globin through naturally occurring suppression of the gamma globin gene. The symptoms of beta-thalassemia and SCD typically do not manifest until several months after birth, when the levels of HbF have declined considerably. Some patients with beta-thalassemia or SCD have elevated levels of HbF that persist into adulthood, a condition known as hereditary persistence of fetal hemoglobin, or HPFH. Patients with HPFH are often asymptomatic, or experience much milder forms of disease. This protective HPFH condition has been shown to result from specific changes to these patients' genomic DNA, either in the region of the globin genes or in certain genetic regulatory elements that control the expression levels of the globin genes.

Relationship between level of HbF and morbidity in beta-thalassemia



An alternative CRISPR/Cas9 approach to treating hemoglobinopathies would be to correct the mutated beta globin gene. We have chosen the HbF upregulation strategy as our initial approach given the relative technical simplicity of the gene deletion strategy involved, the ability of this strategy to counteract a wide variety of different beta globin mutations, and the absence of symptoms in patients with high HbF levels.

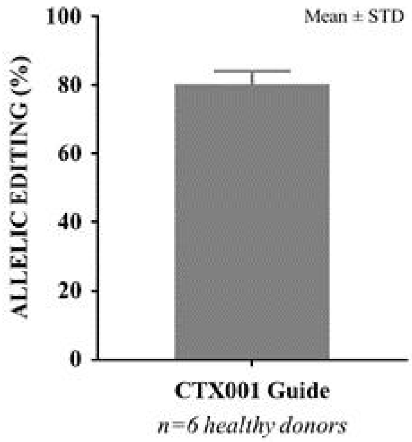
Our Lead Hemoglobinopathies Product Candidate—CTX001

Our lead product candidate, CTX001, uses CRISPR/Cas9 to mimic the high levels of HbF that occur naturally in HPFH patients. To achieve this effect, CTX001 uses CRISPR/Cas9 to disrupt the erythroid specific enhancer of the BCL11A gene. This gene encodes the BCL11A protein, a critical factor that keeps HbF levels low in most individuals. Disrupting the BCL11A erythroid specific enhancer reduces BCL11A expression, thereby upregulating expression of gamma globin and increasing HbF levels.

Our therapeutic approach involves isolating hematopoietic stem cells, or HSCs, which differentiate into red blood cells, from a patient, treating those cells *ex vivo* with CRISPR/Cas9 to disrupt the BCL11A erythroid specific enhancer and reintroducing the edited cells back into the patient. We believe that once reintroduced into the patient, these genetically modified stem cells will give rise to red blood cells that contain high levels of HbF. In beta-thalassemia, elevating HbF may reduce the toxicity of unpaired alpha globin chains, thereby increasing red blood cell lifespan. As a consequence, CTX001 may have the potential to reduce or even eliminate the need for transfusions in these patients. In SCD, elevated HbF may prevent a cell from sickling, and so achieving sufficiently high HbF in a majority of red blood cells could significantly reduce or eliminate the symptoms associated with the disease.

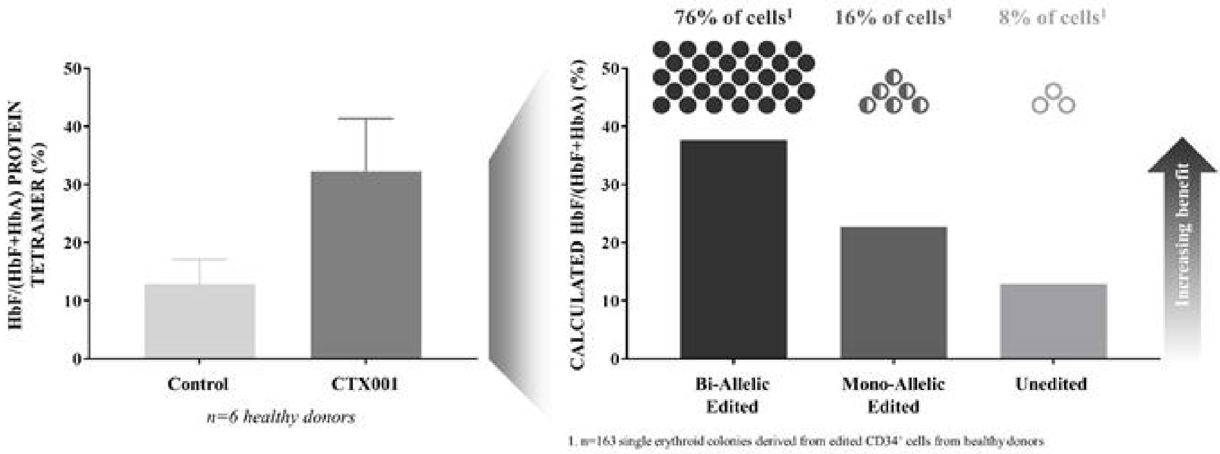
In preclinical studies using CTX001, our CRISPR/Cas9 gene editing process demonstrated the ability to edit HSCs with approximately 80% efficiency at clinical scale in a bulk population of cells.

Editing efficiency at clinical scale in human CD34^{+} cells



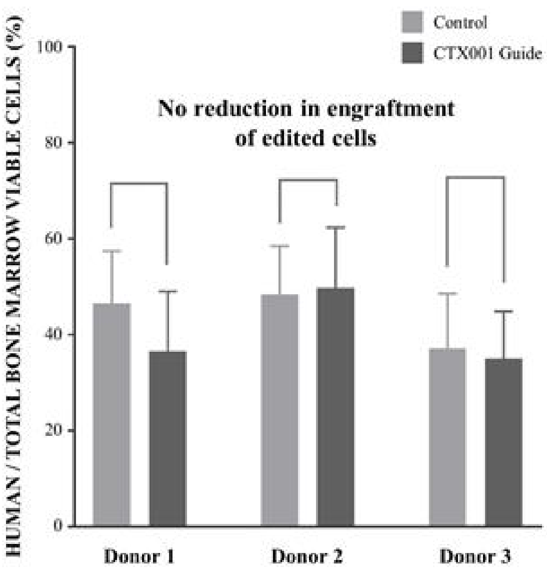
We observed this high editing efficiency across all stem cell subsets, including in long-term repopulating HSCs. After erythroid differentiation, this editing resulted in HbF accounting for greater than 30% of total hemoglobin in edited cells, compared to approximately 10% HbF in the control arm of the study. On a per cell basis, more than 90% of cells had modifications at the desired location, with 76% of the cells having edits in both copies of the target gene, and 16% of the cells having edits made on one copy of the target gene. We estimate that this editing rate results in HbF expression levels of greater than 35% in cells that have edits on both copies of the target gene, and over 20% for cells edited at one gene.

HbF ratio after editing and erythroid differentiation and estimated HbF expression at the cellular level



In preclinical mouse models designed to test the safety of CTX001, gene-edited HSCs maintained the ability to engraft long-term and to differentiate into multiple lineages. Toxicology studies revealed no significant findings and no difference in the biodistribution of edited cells compared to controls. Finally, no off-target activity was detectable for the CTX001 guide RNA after assessing over 5,000 homology-based sites and over 2,000 homology-independent sites.

CTX001 engraftment *in vivo* in mice[1]



1. 16-week engraftment data

In December 2017, we submitted CTAs in major European countries for CTX001 in beta-thalassemia. In March 2018, we received approval of one such CTA and we expect to initiate clinical trials in Europe in 2018. We also expect to file an investigational new drug, or IND, application with the United States Food and Drug Administration, or FDA, for CTX001 in SCD during the first half of 2018. We have designed a single arm Phase 1/2 study in which we plan to enroll up to 30 adult patients to assess the safety and efficacy of CTX001 in patients with beta-thalassemia.

We believe our CRISPR/Cas9 gene editing strategy may have significant advantages over other gene therapies in development for the treatment of hemoglobinopathies. For example, lentivirus-based treatments involve a random integration of one or more copies of the globin gene throughout the genome. The expression levels of the newly introduced gene can vary depending on the exact location of the DNA in the genome, leading to inconsistent and variable levels of expression. We believe our strategy may lead to more uniform globin expression across a high percentage of cells. In addition, with each random lentiviral integration, a mutation may be created, which may have an associated safety concern, including the potential to cause cancer. In contrast, CRISPR/Cas9 targets a specific genomic site for editing, and we have detected no off-target activity for our CTX001 guide RNA.

Other Hematopoietic Programs

There are numerous additional diseases that are potentially treatable through *ex vivo* gene editing of the hematopoietic system. We plan to apply the capabilities we are developing in hemoglobinopathies to treat other diseases, including Hurler Syndrome and severe combined immunodeficiency disease, or SCID.

Hurler Syndrome

Hurler syndrome is a type of mucopolysaccharide disease caused by a defective IDUA gene. The IDUA gene is responsible for encoding alpha-L-iduronidase, an enzyme that breaks down large molecules called glycosaminoglycans, or GAGs, in the lysosomes of cells. A defective IDUA gene results in a lack of alpha-L-iduronidase which leads to an accumulation of GAGs and results in cellular dysfunction and severe clinical abnormalities. Patients with Hurler syndrome have a broad spectrum of clinical problems including skeletal abnormalities, enlarged livers and spleens, and severe intellectual disability due to a lack of this enzyme in the brain. Most patients experience a decline in intellectual development and often lose both vision and hearing as the disease progresses. Without treatment, the average age at death is five years, and nearly all patients die by the age of ten. The worldwide incidence of Hurler syndrome is approximately one in 100,000 births.

There are two common approaches to treating mucopolysaccharide diseases: enzyme replacement therapy and allo-HSCT. Enzyme replacement therapy, or ERT, does not adequately address the symptoms of Hurler syndrome because it cannot cross the blood-brain barrier to address the severe neurologic symptoms associated with this disease. While allo-HSCT can be effective in treating the disease, it is associated with significant morbidity and mortality, and not all patients are able to find suitable donors. Even when a match is found, the delay between diagnosis and treatment often results in significant irreversible disease progression. Our approach is to introduce a functional copy of the IDUA gene into a patient's own hematopoietic cells using *ex vivo* CRISPR/Cas9 gene editing, before returning them to the patient. We believe that using a patient's own cells rather than those from a donor will eliminate a potentially lengthy search for an appropriate donor, allowing us to intervene at an earlier point and avoid the significant risks associated with allo-HSCT.

Severe Combined Immunodeficiency Disease

Severe combined immunodeficiency disease, or SCID, is a disease in which the patient's immune system is compromised and cannot fight off infections. These patients are identified early in life because they often suffer from recurrent severe respiratory infections, which can be life-threatening in the absence of a functioning immune system. There are multiple underlying causes of SCID, and in one particularly severe form, a gene called RAG1 is mutated. Mutations in RAG1, a gene that plays a critical role in the process of antibody generation, prevent normal development of the patient's immune system, resulting in an absence of B-cells, a type of white blood cell. The worldwide incidence of SCID is estimated to be one in 58,000 births, with the RAG1 mutation associated form accounting for approximately 15% of patients.

Currently, the only curative therapy for this potentially fatal disorder is allo-HSCT, which carries a high risk of complications. Gene therapies for SCID insert copies of a replacement gene randomly into the genome, potentially resulting in unwanted mutations. The risks associated with this type of gene therapy were underscored in a clinical trial for another variant of SCID in which five out of twenty patients developed leukemia. We believe that the precise correction of the RAG1 gene with CRISPR/Cas9 may bring benefit to these patients while minimizing the risk of leukemia associated with gene therapy. Considering corrected cells proliferate faster than non-corrected cells, we believe that a small number of corrected cells reintroduced into the patient could provide a therapeutic benefit and in time, compensate for the defective cells. With our *ex vivo* approach, we believe we can attain sufficient levels of correction to generate the desired therapeutic benefit. Our Casebia joint venture with Bayer HealthCare will lead development of our SCID program, and leverage Bayer HealthCare's expertise in hematologic disorders.

Ex Vivo *Immuno-Oncology Programs*

Over the past several years, interest in the oncology community has grown rapidly in the field of immuno-oncology, or treatments that harness the immune system to attack cancer cells. Engineered immune cell therapy is one such approach, in which immune system cells such as T-cells are genetically modified to enable them to recognize and attack cancerous cells.

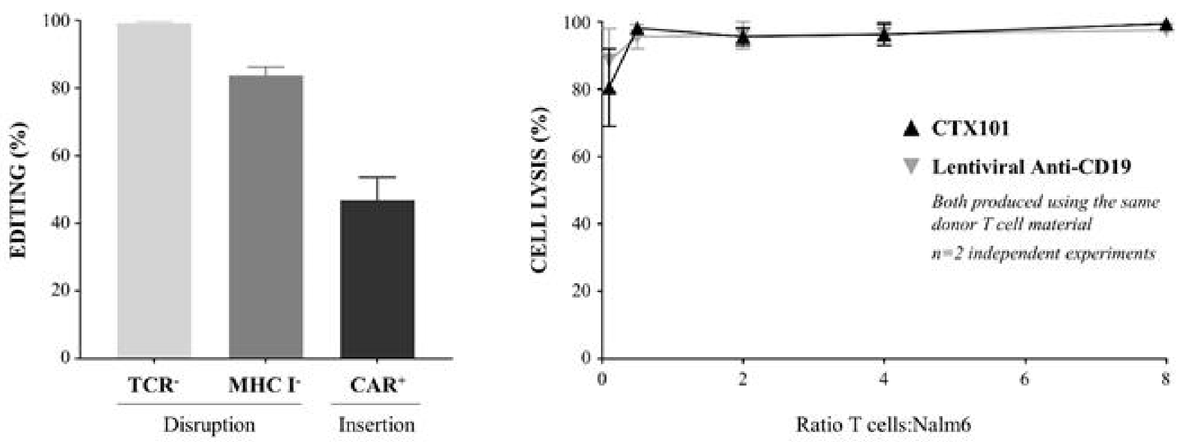
Engineered cell therapy has demonstrated encouraging results leading to two recent approvals for autologous CD19 chimeric antigen receptor T-cell, or CAR-T, products, and may become an entirely new class of oncology therapeutics; however, realizing this full potential will require overcoming some key challenges. Most engineered cell therapies in development require unique products to be created for each patient treated, an approach that has in the past proven challenging and cost prohibitive in the field of oncology. Additionally, these versions of engineered cell therapies appear limited in their ability to treat solid tumors and have demonstrated sub-optimal safety profiles.

We expect that the cellular engineering strategies that are ultimately successful in immuno-oncology will involve multiple genetic modifications, an application for which we believe CRISPR/Cas9 will play a central role. While other gene editing platforms could potentially be used for these purposes, CRISPR/Cas9 is particularly well-suited for multiplexed editing, which is the modification and/or insertion of multiple genes within a single cell. Current gene editing techniques that require different protein enzymes for each genetic modification may be limited in the number of edits they can make concurrently due to efficiency, cytotoxicity, and/or manufacturing challenges. In contrast, CRISPR/Cas9 has the potential to efficiently make multiple edits using a single Cas9 protein and multiple small guide RNA molecules. Given the important role we believe CRISPR/Cas9 will play in engineered cell therapy going forward we have thus far elected to wholly own all of our immune-oncology programs.

Our Lead Immuno-Oncology Product Candidate—CTX101

Our lead immuno-oncology product candidate, CTX101, is a healthy-donor derived allogeneic CAR-T cell product targeting CD19-positive malignancies, such as certain lymphomas and leukemias. A primary aim of CTX101 is to overcome the inefficiency and cost of creating a unique product for each patient in a tumor type by treating many different patients from a single batch, which we refer to as being an "off-the-shelf" therapy. To generate CTX101, we make three modifications to T-cells taken from healthy donors using our CRISPR/Cas9 technology: (i) the T cell receptor, or TCR, is eliminated to reduce the risk of graft versus host disease from the product, (ii) a CD19-directed CAR is inserted site-specifically into the TCR gene and (iii) the class I major histocompatibility complex, MHC-I, is removed from the cell surface in order to improve the persistence of the CAR-T cells in an "off-the-shelf" setting. We believe this approach will have advantages over other allogeneic CAR-T products in development that semi-randomly insert the CAR using an integrating virus, and do not include the MHC-I knockout to increase persistence. As shown in the figure below, we have demonstrated the ability to perform the edits necessary to generate CTX101 at high efficiency, and that in preclinical testing CTX101 has comparable cytotoxic activity to currently approved CD19 CAR-T products. We have transferred production of CTX101 to a GMP-capable contract manufacturing organization ("CMO") and are planning to file an IND for CTX101 by the end of 2018.

Efficient production of CTX101 via multiplexed editing and CTX101 cytotoxic activity *in vitro*



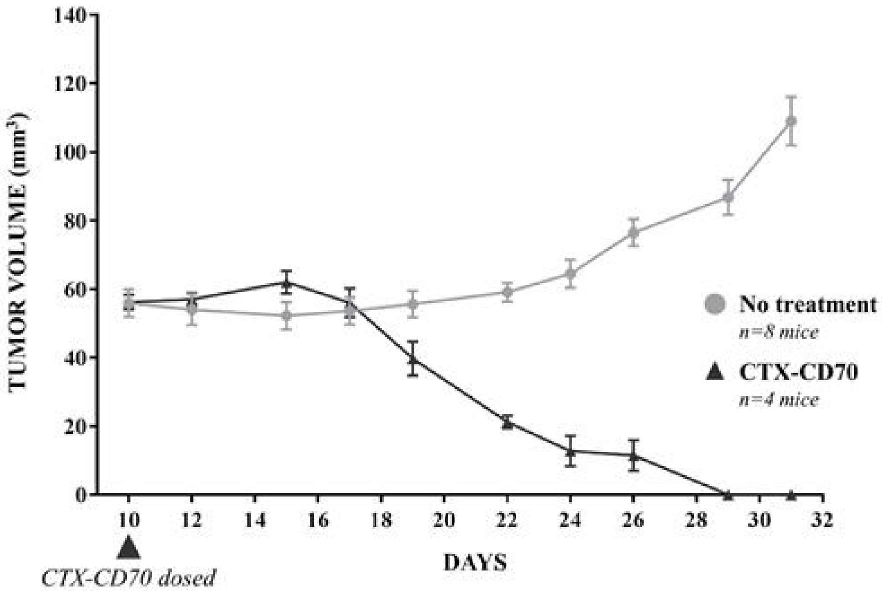
Other Immuno-Oncology Programs

Beyond CTX101, we are developing additional programs directed to other tumor targets including B-cell maturation antigen, or BCMA, and CD70. These programs will leverage many of the capabilities and reagents developed for CTX101, potentially enabling them to progress quickly into development.

BCMA has attractive properties for CAR-T cell therapy, namely expression on the surface of B-lineage cells, especially the plasma cells involved in multiple myeloma, and absence from other tissues and cell types. As a result, BCMA has become a promising target for autologous CAR-T cell therapy. We have tested multiple constructs *in vitro* and *in vivo* in order to select a lead allogeneic CAR-T cell product candidate to progress into development.

CD70 also shows properties that we believe make it a promising CAR-T cell target. A number of cancers express CD70, including non-Hodgkin's lymphoma, renal cell carcinoma, and glioblastoma, while normal tissues do not express or show extremely limited expression of CD70. This target enables us to transition from hematological cancers, such as non-Hodgkin's lymphoma, to solid tumor cancers, such as renal cell carcinoma. In preclinical studies of an allogeneic CAR-T cell product candidate directed against CD70, we observed promising anti-tumor activity, including the complete eradication of tumors in a mouse model of renal cell carcinoma.

Elimination of a subcutaneous A498 renal cell carcinoma model by allogeneic anti-CD70 CAR-T cells (CTX-CD70)



In these and future programs, we may use the multiplexing ability of CRISPR/Cas9 to introduce additional genetic edits to improve the efficacy and safety profile of these products. Such edits could include the removal of checkpoint inhibitors or introduction of safety elements. We continue to expand our multiplexing capabilities through platform development in order to help us realize the full potential of engineered cell therapy in immuno-oncology across all tumor types, including solid tumors.

In Vivo Programs

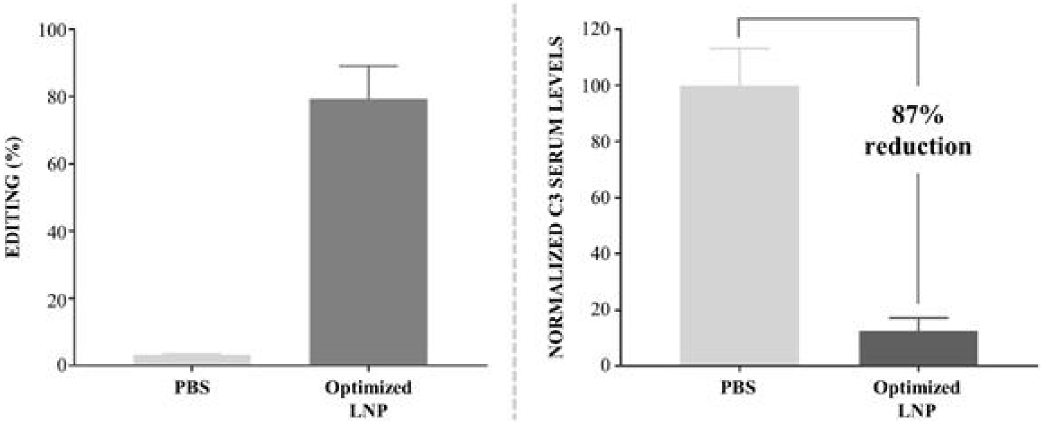
In parallel with our *ex vivo* programs, we are pursuing a number of *in vivo* indications, which will involve delivery of CRISPR/Cas9-based therapeutics directly to tissues within the human body. Our initial *in vivo* applications will target the liver, leveraging well-established delivery technologies. We have also begun optimizing delivery systems to target other organ systems, including musculoskeletal and pulmonary.

Liver Diseases

We have selected liver diseases as our initial *in vivo* targets because delivery of nucleic acid therapies into the liver has been clinically established and validated delivery technologies are now available, including, but not limited to, lipid nanoparticle-based delivery vehicles, or LNPs, and adeno-associated viral vectors, or AAV vectors. We believe this proof of concept reduces the challenges associated with delivering CRISPR/Cas9-based therapeutics *in vivo* to the liver.

We have observed promising preclinical results in our studies with both viral and non-viral delivery technologies. For example, using LNPs, we were able to demonstrate approximately 80% editing rates in mouse models at the target gene which resulted in greater than 85% reduction in the expression of the gene as measured by protein levels in the serum, as shown in the figure below.

Significant decrease in serum C3 levels after editing *in vivo*[1]



1. Editing and serum protein quantified in five mice following intravenous LNP dose

Within the liver we are pursuing diseases that have well understood genetic linkages and have begun preclinical development for multiple indications including glycogen storage disease Ia, or GSDIa, and hemophilia. In both of these indications, evidence suggests that correction of the mutant gene in only a small percentage of liver cells may have a significant therapeutic effect, which makes the gene correction strategy feasible in these indications.

Glycogen Storage Disease Ia

Overview

GSDIa, also known as Von Gierke disease, is an autosomal recessive inborn error of glucose metabolism caused by a mutation in the G6PC gene, which encodes the glucose-6-phosphatase protein, or G6Pase. In patients with GSDIa, the lack of G6Pase prevents the release of glucose from the liver, resulting in accumulation of a large chain form of glucose known as glycogen. The inability of patients with GSDIa to regulate glucose levels leads to hypoglycemia, or low blood glucose, and high levels of lactic acid when patients are not eating, requiring patients to adhere to burdensome dietary regimes. GSDIa patients also face long-term risks such as growth delay, neuropathy and kidney stones. Additionally, due to the accumulation of glycogen in the liver, 70% to 80% of patients over 25 years of age will develop hepatocellular adenomas, a type of non-cancerous growth in the liver, of which approximately 10% will progress to hepatocellular carcinoma, a potentially fatal liver cancer. There are approximately 1,000 new cases of GSDIa per year worldwide.

Limitations of Current Treatment Options

There are currently no disease-modifying treatment options for patients with GSDIa. Any disruption in carbohydrate delivery may lead to low blood sugar levels, which can cause life-threatening consequences including seizure, coma and death. To minimize the risk of acute complications, patients are required to adhere to highly burdensome, lifelong dietary regimens such as overnight administration of uncooked cornstarch or a slow-release carbohydrate product such as Glycosade. These regimens have a high rate of non-compliance, leading to increased risk of serious long-term complications.

Our Gene Editing Approach

We are developing a CRISPR/Cas9 product candidate to correct the mutation in GSDIa patients. Animal model experiments have demonstrated that the addition of functional copies of the G6PC gene is capable of correcting the deficiency of G6Pase protein in GSDIa and that as little as 3% of normal levels of G6Pase can restore the equilibrium of glucose and glycogen in the bloodstream and liver. Our approach is to correct the G6PC gene directly in its native location. We believe this direct gene correction will result in appropriate expression of the G6Pase protein. Other methods rely on adding copies of the gene through viral delivery methods, which we believe may lead to overexpression of the G6Pase protein and ineffective control of glucose levels.

Hemophilia

Overview

Hemophilia is an X-linked recessive genetic disease primarily present in male children. Our initial hemophilia program targets hemophilia B, which results from a deficiency in factor IX, an enzyme produced in the liver. Factor IX is part of the blood coagulation system, which enables blood to form clots in response to injury and bleeding. A lack of factor IX leads to an increased risk of bleeding, either spontaneously or in response to injury.

Patients with severe forms of the disease are first diagnosed at infancy, as witnessed through prolonged bleeding from simple medical procedures or through excessive bruising from simple falls. These patients have frequent spontaneous bleeding into joints and muscles, which can lead to edema, inflammation and debilitating pain. Patients with mild forms of the disease typically present as normal, and diagnosis usually follows surgery or trauma. The worldwide prevalence of hemophilia B patients is estimated to be 28,000, including over 4,000 in the United States. About half of hemophilia B cases are classified as severe based on levels of factor IX activity that are less than 1% of normal.

Limitations of Current Treatment Options

The standard of care for symptomatic patients with hemophilia B involves enzyme replacement with recombinant factor IX. Exogenous factor IX protein is administered both as a prophylaxis and during acute bleeding episodes. While considered effective, factor IX replacement therapies are invasive, inconvenient and non-curative. Until recently, hemophilia B therapy required weekly intravenous injections or infusions. While administration frequency has improved in recent years, key drawbacks of protein therapy, including fluctuations in factor IX levels, remain a significant pitfall of enzyme replacement therapies.

Our Gene Editing Approach

We believe that hemophilia B symptoms can be dramatically reduced with only a moderate restoration in factor IX activity. It has been shown that patients with more than 5% of normal factor IX activity have milder forms of the disease and may not present symptoms in the absence of trauma or surgery. This observation implies that in patients with severe forms of the disease, restoration of factor IX activity to a level of 5% or more of normal may be clinically meaningful.

The correction of a mutant factor IX gene with CRISPR/Cas9 leverages endogenous regulation via correction of the gene at its native location within the genome. As a result, we believe it may represent a superior way to treat hemophilia B patients, relative to other gene therapy approaches that insert the correct gene at a random location in the genome. Our hemophilia program will be developed within the Casebia joint venture, leveraging Bayer’s expertise in this disease area together with our gene editing expertise.

Other Organs

In addition, we have initiated several *in vivo* programs targeting diseases of organ systems outside the liver, such as Duchenne muscular dystrophy, or DMD, and cystic fibrosis, or CF. In CF, we are working with Vertex, a global leader with extensive disease area expertise. We believe that our CRISPR/Cas9 gene editing technology is well suited to address these diseases, both of which have significant patient populations with high unmet medical need.

Duchenne Muscular Dystrophy

Overview

Duchenne muscular dystrophy is an X-linked recessive genetic disease caused by a mutation in the dystrophin gene, which results in a lack of the dystrophin protein, a protein that plays a key structural role in muscle fiber function. The absence of dystrophin in muscle cells leads to significant cell damage and ultimately causes muscle cell death and fibrosis. DMD is characterized by muscle degeneration, loss of mobility and premature death, and is among the most prevalent severe genetic diseases, occurring in one in 3,300 male births worldwide. There is also a related form of muscular dystrophy called Becker muscular dystrophy, or BMD, which is also caused by mutations in the dystrophin gene. However, unlike DMD, the mutations in BMD result in the loss of certain exons or regions of the gene and can lead to an abnormal version of dystrophin that retains some function. As a result, BMD patients have milder symptoms than DMD patients.

There is currently one approved disease-modifying therapy in the United States for the treatment of DMD in patients who have a confirmed mutation of the dystrophin gene amenable to exon 51 skipping, which affects about 13% of the population with DMD. This therapy involves the use of oligonucleotides to promote exon skipping over the mutations that otherwise would result in truncated dystrophin synthesis. While exon skipping has demonstrated promising results in limited settings, larger clinical trials of this approach have suggested only modest efficacy. In addition, delivering sufficient levels of oligonucleotides requires repeated administration and presents challenges to treating DMD.

Our Gene Editing Approach

We are pursuing multiple approaches to developing therapies for DMD. Our first approach is to deliver CRISPR/Cas9 directly to muscle cells in patients to delete the defective exons in the dystrophin gene. The goal of this approach is to allow the gene to regain some functional capacity and produce enough dystrophin protein to diminish the more severe symptoms of DMD to resemble the milder form of the disease known as BMD. We believe that currently available technology is capable of delivering the CRISPR/Cas9 into muscle cells, and together with the relatively high efficiency of exon deletion using the CRISPR/Cas9 system, we will be able to move this program into clinical testing.

In parallel, we are performing *in vitro* experiments to test the principle of dystrophin gene correction which could potentially be curative. Prior studies in mice and humans have indicated that dystrophin levels as low as 4 to 15% of normal are sufficient to ameliorate symptoms, suggesting that even a partial restoration of dystrophin levels would be therapeutically beneficial.

Cystic Fibrosis

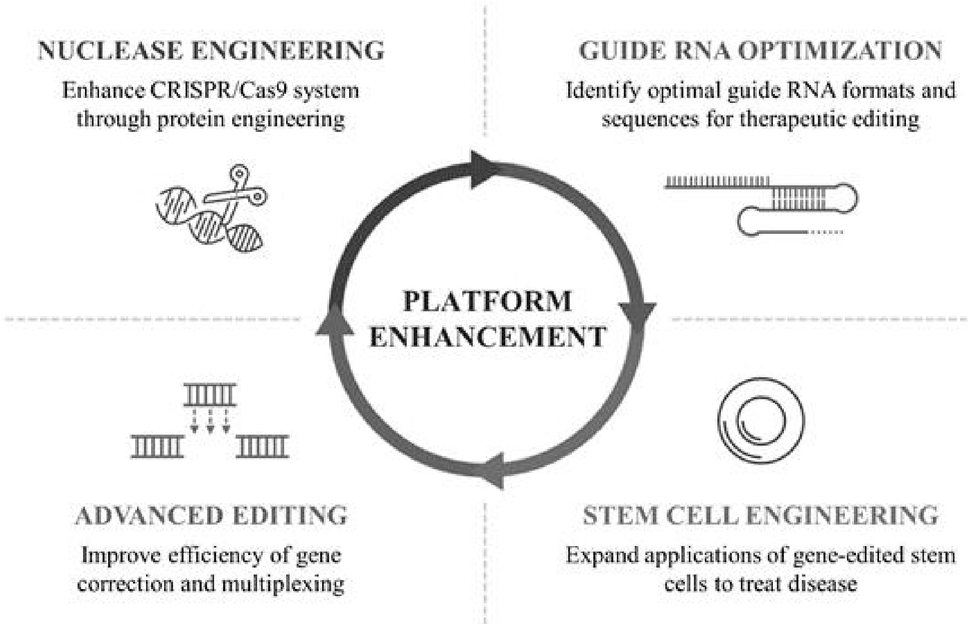
Cystic fibrosis is a progressive disease caused by mutations in the cystic fibrosis transmembrane regulator, or CFTR, gene resulting in the loss or reduced function of the CFTR protein. Although there are several different mutations associated with CF, approximately 70% of CF patients have the same mutation at codon 508 of the CFTR gene. Patients with CF develop thick mucus in vital organs, particularly in the lungs, pancreas and gastrointestinal tract. As a result, CF patients experience chronic severe respiratory infections, chronic lung inflammation, poor absorption of nutrients, progressive respiratory failure and early mortality.

CF is an orphan disease that affects an estimated 70,000 to 100,000 patients worldwide, with a majority in the United States and Europe. The median age of death from CF in the United States in 2015 was 29 years, with most deaths resulting from respiratory failure. CF patients require lifelong treatment with multiple daily medications and hours of self-care. They often require frequent hospitalizations and sometimes even lung transplantation, which can prolong survival but is not curative.

Studies have shown that as little as 10% of normal CFTR function can ameliorate disease symptoms. Our approach is focused on using our CRISPR/Cas9 technology to correct mutations in the CFTR gene. Together with our collaboration partner Vertex, we believe that we will be able to deliver CRISPR/Cas9 to the lung and correct this mutation sufficiently to improve symptoms in patients with CF.

Further Unlocking the Potential of Our CRISPR/Cas9 Platform

We are working to optimize our CRISPR/Cas9 platform. Our key areas of focus are described below.



Nuclease Engineering

The Cas9 nucleases found in nature are highly efficient and specific. We believe that for many gene-editing applications, the naturally occurring Cas9 variants have all the properties required to support an effective therapeutic. However, we also see potential in certain disease areas and organ systems where modified versions of Cas9 may be more effective, and we are working internally and through our external collaborations to develop these.

Our research and development efforts seek to enhance a number of characteristics of Cas9, including size, specificity, immunogenicity and ability to support different types of editing strategies. We believe that the process of optimizing these different parameters may yield a number of effective Cas9 versions with different properties, each of which may be best suited to a certain disease area or type of genetic editing.

Guide RNA Optimization

Selecting the sequence for guide RNAs is a critical step in the process of designing our product candidates. Once we have chosen a gene editing strategy, we seek to identify guide RNAs that will perform the desired edit with high efficiency and with extremely low off-target cutting. While computational models can predict efficiency and off-target effects with reasonable accuracy, we believe that a combination of computation and experimental approaches is necessary to reliably select the best possible guide RNAs.

Our guide RNA selection process combines bioinformatics and experimental assays to enable the screening of large numbers of guide RNAs in each experiment. This process starts with proprietary bioinformatics algorithms that select a large pool of guide RNAs that are predicted to have desired properties. These guides are then tested for target site cutting efficiency using a high-throughput screening platform in a model cell line. The most efficient guides are then put through two screening processes for possible off-target effects. First, bioinformatics algorithms are used to identify the 10 to 20 sites in the genome that are most likely to show off-target effects, and these sites are examined through high-throughput assays for empirical off-target cutting. Second, homology-independent screening is performed to identify any potential off-target cutting, even at unpredicted locations. Finally, a small subset of guides with the highest efficiency and lowest off-target potential are tested in the cell type of therapeutic interest before choosing a lead guide or guides for our program.

Advanced Editing

While gene correction is achievable today using CRISPR/Cas9, it is more difficult and has lower efficacy than the more straightforward gene disruption strategy. Our initial gene correction programs target diseases in which therapeutic efficacy can be achieved through correction of only a small percentage of cells, while other potential indications may require correction of a significantly higher percentage of cells. We are working with our collaborators to increase the efficiency of gene correction in order to facilitate the potential treatment of these additional indications.

A central focus of our development efforts is to optimize the correction rates in cell types where rates of correction are typically low. Some of this optimization is being done internally, to test the influence of different parameters of the CRISPR/Cas9 system on correction efficiency. In addition, we are advised by Dr. Stephen Elledge, Professor of Genetics at Harvard Medical School, who is an expert in DNA damage and repair, to explore ways to optimize the cellular processes involved in the correction process. We are also collaborating more broadly with leaders in the DNA repair field, to explore other approaches to optimize correction rates.

We are also focused on expanding our ability to perform multiple edits simultaneously. In contrast to other gene editing technologies, which require extensive protein engineering and an additional construct for each new genetic target, CRISPR/Cas9 only requires a new guide RNA using simple Watson-Crick base pairing to target a new genetic locus. As a result, one can easily perform many edits at once using CRISPR/Cas9, a process known as multiplexing. Multiplexing holds particular promise in cellular therapies, where making several modifications may lead to a safer and more efficacious therapy. Our research efforts in this area emphasize developing strategies to keep editing rates high while multiplexing without increasing the risk of off-target activity.

Stem Cell Engineering

Many *ex vivo* applications of our technology use a strategy of editing stem cells *ex vivo* which, when returned to the patient, differentiate into a variety of different cell types. For certain stem cell types, especially hematopoietic cells, there are well-established procedures to support this strategy. For others, these procedures are more nascent and require further development. A critical focus for us is to improve the efficacy, efficiency and safety of the *ex vivo* cell collection, manipulation and administration process for a variety of stem cell types. We are evaluating technologies to improve mobilization of a patient’s stem cells, to maintain viability of the harvested cells and to improve the ability of these cells to engraft into a patient’s body. Both in our own laboratories and through our academic partnerships, we intend to perform additional research to optimize these parameters for each organ system.

Strategic Partnerships and Collaborations

We intend to develop CRISPR/Cas9-based therapeutics both independently and in collaboration with current and potential future corporate partners. We view strategic partnerships as a core component of our strategy, allowing us to access capabilities and resources in support of our therapeutic programs. We have established two broad strategic partnerships – a research collaboration with Vertex Pharmaceuticals Incorporated and a joint venture with Bayer HealthCare – to develop gene-editing-based therapeutics in specific disease areas. Our partnerships with Bayer and Vertex provide over $400 million, inclusive of estimated spending on funded programs, which will be used to advance the programs included in these partnerships.

Under our agreement with Bayer HealthCare, we established Casebia Therapeutics LLP, or Casebia, a joint venture in which we and Bayer HealthCare are equal owners. We and Bayer intend for Casebia to largely focus on more challenging *in vivo* therapeutic areas in larger patient populations, and to invest resources in optimizing the platform and delivery technologies for *in vivo* delivery. Through our agreement, we will have access to technology enhancements developed or obtained by Casebia for the benefit of our other wholly owned programs.

Our agreement with Vertex is a two-part collaboration. We granted Vertex an option to co-develop and co-commercialize rights to the hemoglobinopathies program and options to license certain other programs with the potential to receive milestone payments and royalties. Since signing the original agreement, Vertex has exercised their option to co-develop and co-commercialize the hemoglobinopathies program for which net profits and losses, as applicable, will be shared equally by the parties.

Enabling Technologies

In support of our lead *ex vivo* programs, we have entered into a commercial license agreement with MaxCyte Incorporated. The license provides CRISPR and Casebia a non-exclusive commercial-use right to MaxCyte's cell engineering platform to develop CRISPR/Cas9-based therapies for hemoglobin-related diseases and severe combined immunodeficiency. Our lead program, CTX001, utilizes MaxCyte's Flow Electroporation™ Technology to deliver CRISPR/Cas9 components to hematopoietic stem cells.

We have also formed several collaborations to support our *in vivo* programs. Together with Casebia, we have a collaboration with CureVac AG to develop novel Cas9 mRNA constructs with improved properties for gene editing in the liver, such as increased potency, decreased duration of expression and reduced potential for immunogenicity. As part of the collaboration, CureVac will provide mRNA manufacturing through clinical development and commercialization.

We have also entered into a development and option agreement with StrideBio LLC to develop novel AAV vectors for *in vivo* gene editing applications. Under the agreement, StrideBio will use its proprietary structure-guided evolution platform to develop AAV vectors with improved properties, such as tissue specificity and reduced susceptibility to immune responses. Under this agreement we have the option to exclusively license AAV vectors with desired properties for certain of our *in vivo* programs.

Additionally, we have access to non-viral delivery technology through an exclusive license from the Massachusetts Institute of Technology to a family of LNP technologies developed in the lab of Dr. Daniel G. Anderson, a scientific founder and advisory board member of CRISPR Therapeutics.

Academic and Discovery Collaborations

We have a two-year research collaboration and license option agreement with Massachusetts General Hospital Cancer Center, or MGHCC, to develop novel T cell therapies for cancer. Marcela V. Maus, MD, PhD, Director of the Cellular Immunotherapy Program at MGHCC and Assistant Professor of Medicine at Harvard Medical School, will lead the scientific work at MGHCC. The research will involve using CRISPR/Cas9 gene editing to improve upon current T cell therapies in development, ultimately addressing unmet needs in both hematologic and solid tumors.

Also in the immuno-oncology space, we have a research collaboration with Neon Therapeutics, an immuno-oncology company developing neoantigen-based therapeutic vaccines and T cell therapies to treat cancer. The collaboration combines our respective proprietary technologies to explore the development of novel T cell therapies.

We and our collaborators at the University of Florida, or UF, have received a two-year grant from Target ALS Foundation to support preclinical discovery and validation of CRISPR/Cas9-based therapeutic approaches directed to ALS and frontotemporal dementia. We will collaborate with Dr. Laura Ranum and Dr. Eric Wang at UF to test CRISPR/Cas9 gene editing strategies in animal models of the disease.

We also received the Kyle Bryant Translational Research Award from Friedreich's Ataxia Research Alliance, or FARA, a non-profit organization that is focused on curing Friedreich's Ataxia, or FA. The grant will fund research on *in vivo* CRISPR/Cas9-based gene-editing approaches to treat FA, which we will conduct in collaboration with Dr. Marek Napierala at University of Alabama at Birmingham.

Intellectual Property

We strive to protect and enhance the proprietary technologies that we believe are important to our business by seeking patents to cover our platform technology, which consists of the in-licensed intellectual property of Dr. Emmanuelle Charpentier described below, including compositions of matter and their therapeutic uses. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for our technology, our ability to defend and enforce our intellectual property rights and our ability to operate without infringing any valid and enforceable patents and proprietary rights of third parties.

In-Licensed Intellectual Property

In April 2014, pursuant to an exclusive license with Dr. Emmanuelle Charpentier, we licensed from Dr. Charpentier certain rights to a family of patent applications relating to compositions of matter, including additional CRISPR/TRACR/Cas9 complexes, and methods of use, including their use in targeting or cutting DNA. This license is limited to therapeutic products such as pharmaceuticals and biologics and any associated companion diagnostics, for the treatment or prevention of human diseases, disorders, or conditions. For further information about this license, please see "Business – CRISPR License with Dr. Emmanuelle Charpentier."

This family of patent applications includes approximately eight (8) granted or allowed patents in the United Kingdom, Europe, China, New Zealand, Singapore, Australia and Mexico, and pending patent applications in the United States, Europe, Canada, Mexico, Australia and other selected countries in Central America, South America, Asia and Africa. The granted patents and any other patents that may ultimately issue in this patent family are expected to expire in 2033, not including any applicable extensions.

In addition to Dr. Emmanuelle Charpentier, this family of patent applications has named inventors who assigned their rights either to the Regents of the University of California, or California, or the University of Vienna, or Vienna. California's rights are subject to certain overriding obligations to the sponsors of its research, including the Howard Hughes Medical Institute and the U.S. Government. Caribou Biosciences, or Caribou, had reported that it had an exclusive license to patent rights from California and Vienna, subject to a retained right to allow non-profit entities to use the inventions for research and educational purposes. Intellia Therapeutics, Inc., or Intellia, had reported that it had an exclusive license to such rights from Caribou in certain fields.

In January 2016, the U.S. Patent and Trademark Office, or USPTO, declared an interference between one of the pending U.S. patent applications in this family and twelve issued U.S. patents owned jointly by the Broad Institute and Massachusetts Institute of Technology and, in some instances, the President and Fellows of Harvard College, which we refer to individually and collectively as Broad. The interference was redeclared in March 2016 to add a U.S. patent application owned by Broad. An interference is a proceeding conducted at the USPTO by the Patent Trial and Appeal Board, or PTAB, to determine which party was the first to invent subject matter claimed by at least two parties. There are currently two parties to this interference. The USPTO designated Dr. Emmanuelle Charpentier, California and Vienna collectively as "Senior Party" and designated Broad as "Junior Party." Following motions by the parties and other procedural matters, the PTAB concluded in February 2017 that the declared interference should be dismissed because the claim sets of the two parties were not directed to the same patentable invention in accordance with the PTAB's two-way test for patent interferences. In particular, the Junior Party's claims in the interference were all limited to uses in eukaryotic cells, while the Senior Party's claims in the interference were not limited to uses in eukaryotic cells but included uses in all settings. Senior Party has appealed the decision to the U.S. Court of Appeals for the Federal Circuit. In parallel, either party can also pursue existing or new patent applications in the U.S. and elsewhere. Going forward, either party as well as other parties could seek a new interference related to the uses of the technology in eukaryotic cells or other aspects of the technology, and any existing or new patents could be the subject of other challenges to their validity of enforceability. If there is a second interference, either party could again appeal an adverse decision to the U.S. Court of Appeals for the Federal Circuit. In any case, it may be years before there is a final determination on priority. Pursuant to the terms of the license agreement with Dr. Charpentier, we are responsible for covering or reimbursing Dr. Charpentier's patent prosecution, defense and related costs associated with our in-licensed technology. For further information regarding risks regarding the interference and patent rights held by third parties, please see "Risk Factors—Risks Related to Our Intellectual Property."

On December 15, 2016, we entered into a Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement, or the IMA, with California, Vienna, Dr. Charpentier, Intellia, Caribou, ERS Genomics Ltd., or ERS, and TRACR. Under the IMA, California and Vienna retroactively consent to Dr. Charpentier's licensing of her rights to the CRISPR/Cas9 intellectual property, pursuant to our license with Dr. Charpentier, to us, our wholly-owned subsidiary TRACR, and ERS, in the United States and globally. The IMA also provides retroactive consent of co-owners to sublicenses granted by us, TRACR and other licensees, prospective consent to sublicenses they may grant in future, retroactive approval of prior assignments by certain parties, and provides for, among other things, (i) good faith cooperation among the parties regarding patent maintenance, defense and prosecution, (ii) cost-sharing arrangements, and (iii) notice of and coordination in the event of third-party infringement of the subject patents and with respect to certain adverse claimants of the CRISPR/Cas9 intellectual property. Unless earlier terminated by the parties, the IMA will continue in effect until the later of the last expiration date of the patents underlying the CRISPR/Cas9 technology, or the date on which the last underlying patent application is abandoned. For further information regarding the effects of joint ownership in the United States and in other jurisdictions worldwide, please see "Risk Factors – *The Intellectual Property That Protects Our Core Gene Editing Technology Is Jointly Owned, And Our License Is From Only One Of The Joint Owners, Materially Limiting Our Rights In The United States And In Other Jurisdictions*."

CRISPR-Owned Intellectual Property

We also own over 40 families of patent applications relating to our platform technology or its therapeutic applications. These patent applications are currently pending in the United States and in some cases in other countries, and we may elect to pursue additional related applications internationally. Any patents that ultimately issue from these patent applications may begin to expire in 2034.

Patent Assignment Agreement

In November 2014, we entered into a patent assignment agreement with Dr. Emmanuelle Charpentier, Dr. Ines Fonfara and Vienna, or the Patent Assignment Agreement. Under the Patent Assignment Agreement, Dr. Charpentier, Dr. Fonfara and Vienna assigned to us all rights to a family of patent applications relating to certain compositions of matter, including additional CRISPR/TRACR/Cas9 complexes, and methods of use, including their use in targeting or cutting DNA.

As consideration for the patent rights assigned to us, we agreed to pay an upfront payment, milestone payments beginning with the filing of a U.S. Investigational New Drug application or its equivalent in another country, a minimum annual royalty, a low single-digit royalty on net sales of products whose manufacture, use, sale, or importation is covered by the assigned patent rights, and a low single-digit percentage of licensing revenues.

We are obliged to use commercially reasonable efforts to obtain regulatory approval to market a product whose manufacture, use, sale, or importation is covered by the assigned patent rights, including but not limited to an obligation to use commercially reasonable efforts to file a U.S. Investigational New Drug application (or its equivalent in a major market country) by November 2021.

License Agreements

CRISPR License With Dr. Emmanuelle Charpentier

In April 2014, we entered into a license agreement, or the Charpentier License Agreement, with Dr. Emmanuelle Charpentier, one of our co-founders, pursuant to which we received an exclusive license under Dr. Charpentier's joint ownership interest a family of patent applications relating to CRISPR/TRACR/Cas9 complexes and their use in targeting or cutting DNA, which we refer to as the Patent Rights, to research, develop and commercialize therapeutic products such as pharmaceuticals or biological preparations, and any associated companion diagnostics, for the treatment or prevention of human diseases, disorders, or conditions, other than hemoglobinopathies, which we refer to as the CRISPR Field. The license is exclusive, even as to Dr. Charpentier, except that she retains a non-transferable right to use the technology for her own research purposes and in research collaborations with academic and non-profit partners. The exclusive license is granted only under Dr. Charpentier's interest in the patent applications and the exclusivity is not granted under any other joint owner's interest. Additionally, the Charpentier License Agreement granted us an exclusive, worldwide, royalty-free sublicense, including the right to sublicense, to research, develop, produce, commercialize and sell therapeutic products relating to the CRISPR Field which incorporate any intellectual property that TRACR Hematology Ltd., our wholly-owned subsidiary, or TRACR, develops under its license with Dr. Charpentier. In turn, we granted to Dr. Charpentier an exclusive license with the obligation to sublicense to TRACR any intellectual property we develop under the license with Dr. Charpentier for treatment and prevention of hemoglobinopathies in humans, including, without limitation, sickle cell disease and thalassemia.

Under the terms of the Charpentier License Agreement, as consideration for the license, Dr. Charpentier received a technology transfer fee, an immaterial annual maintenance fee, immaterial milestone payments that will be due after the initiation of clinical trials, a low single digit percentage royalty on net sales of licensed products, and a low single digit percentage royalties of sublicensing revenue. We are obligated to use commercially reasonable efforts to obtain regulatory approval to market a licensed therapeutic product. CRISPR must use commercially reasonable efforts to file a U.S. Investigational New Drug application (or its equivalent in a major market country for a therapeutic product in the CRISPR field) by April 2021. In addition, CRISPR must file a U.S. Investigational New Drug application (or its equivalent in a major market country) for a therapeutic product in the CRISPR field by April 2024.

Unless terminated earlier, the term of the Charpentier License Agreement will expire on a country-by-country basis, upon the expiration of the last to expire valid claim of the Patent Rights in such country. We have the right to terminate the agreement at will upon 60 days' written notice to Dr. Charpentier. We and Dr. Charpentier may terminate the agreement upon 90 days' notice in the event of a material breach by the other party, which is not cured during the 90-day notice period. Dr. Charpentier may terminate the license agreement immediately if we challenge the enforceability, validity, or scope of any Patent Rights.

TRACR License With Dr. Emmanuelle Charpentier

In April 2014, concurrently with our license agreement with Dr. Emmanuelle Charpentier, TRACR Hematology Ltd., our wholly- owned subsidiary, entered into a license agreement, or the TRACR License Agreement, with Dr. Charpentier, a minority shareholder of TRACR, under the Patent Rights. Pursuant to the TRACR License Agreement, TRACR was granted an exclusive, worldwide, royalty-bearing license, including the right to sublicense, to research, develop, produce, commercialize and sell therapeutic and diagnostic products for the treatment and prevention of hemoglobinopathies in humans, including sickle cell disease and thalassemia, or the TRACR Field. TRACR also received a non-exclusive, worldwide, royalty-free license, including the right to sublicense, to carry out internal pharmaceutical research for therapeutic products outside of the TRACR Field and an exclusive, worldwide, royalty-free sublicense, including the right to sublicense, to research, develop, produce, commercialize and sell therapeutic products relating to the TRACR Field which incorporate any intellectual property that CRISPR develops under its license with Dr. Charpentier. In turn, TRACR granted to Dr. Charpentier an exclusive license to sublicense to CRISPR any intellectual property that TRACR develops under the license with Dr. Charpentier for use in the CRISPR Field.

TRACR is obligated to use commercially reasonable efforts to research, develop, and commercialize at least one therapeutic product for the prevention or treatment of human disease under the license agreement. TRACR must use commercially reasonable efforts to file a U.S. Investigational New Drug application (or its equivalent in a major market country) for a therapeutic product in the TRACR field by April 2021. In addition, TRACR must file a U.S. Investigational New Drug application (or its equivalent in a major market country) for a therapeutic product in the TRACR field by April 2024. TRACR is solely responsible for all clinical, regulatory and development costs.

Under the TRACR License Agreement, Dr. Emmanuelle Charpentier is entitled to receive immaterial clinical and regulatory milestone payments per product that TRACR commercializes. TRACR is also required to pay Dr. Charpentier low single digit percentage royalties on the net sales of any approved therapeutic or diagnostic products, made by it, its affiliates, or its sublicensees and low single-digit percentage royalties on sublicensing revenue.

Unless terminated earlier, the term of the license agreement will expire on a country-by-country basis, upon the expiration of the last to expire valid claim of the Patent Rights in such country. TRACR has the right to terminate the agreement at will upon 60 days' written notice to Dr. Emmanuelle Charpentier. TRACR and Dr. Charpentier may terminate the agreement upon 90 days' notice in the event of a material breach by the other party, which is not cured during the 90-day notice period. Dr. Charpentier may terminate the license agreement immediately if TRACR challenges the enforceability, validity, or scope of any Patent Right.

Bayer Joint Venture

In December 2015, we entered into a Joint Venture Agreement, or the JV Agreement, with Bayer HealthCare LLC, or Bayer HealthCare, to create Casebia Therapeutics LLP, or Casebia, to discover, develop and commercialize new therapeutics for genetically linked diseases, including blood disorders, blindness and heart disease. At the closing of the transactions contemplated by the JV Agreement in March 2016, or the Closing, we contributed $0.1 million to Casebia and we and certain of our affiliates entered into an intellectual property contribution agreement with Casebia, or the CRISPR IP Contribution Agreement, as discussed below, exclusively licensing our CRISPR/Cas technology to Casebia for the purpose of developing and commercializing therapeutic products in certain specified fields, or the Casebia Fields. Bayer HealthCare contributed an initial amount of $45 million at the Closing to Casebia and is committed to contribute up to an additional $255 million in additional funds over time to fund the operations of Casebia, subject to the conditions and procedures discussed below. We and Bayer HealthCare each hold a 50%, non-transferable interest in Casebia.

Casebia's initial focus will be within the areas of hematology, ophthalmology and cardiology and autoimmune diseases, in addition to select indications related to other sensory organs and metabolic diseases. Within these areas of focus, we and Bayer HealthCare each have exclusive rights to specified disease indications, the CRISPR Field and Bayer Field, respectively, as discussed below.

Governance

In November of 2016, Casebia appointed James Burns as chief executive officer, or CEO, of Casebia, replacing Axel Bouchon, the head of LifeScience Center of Bayer AG, who was serving as interim CEO. Dr. Burns also joined the Casebia Board as a non-voting member. Casebia is generally governed by a management board, or the Management Board, which is comprised of six voting members, three of which are designated by us and three of which are designated by Bayer. We have designated Drs. Novak, Kulkarni and Ho to serve as our designees to the Management Board. Decisions of the Management Board are generally made by majority vote, with each member having one vote. Certain matters require the consent of Bayer HealthCare and us.

Budget and Funding

The JV Agreement sets forth the initial 24-month budget for Casebia, which will be revised by the Management Board on a yearly basis for the following 24 months. Bayer HealthCare, subject to certain conditions, is solely responsible for providing Casebia with the necessary additional funding as determined by the Management Board until the earlier of (i) its aggregate additional commitment amount of $255 million is fully funded, at which point all additional financing must be approved by the Management Board or (ii) the termination of the JV Agreement in accordance with its terms. Any additional funding beyond the amounts initially committed by Bayer HealthCare in the JV Agreement up to the $300 million aggregate commitment amount, whether for purposes of an acquisition or otherwise, will not affect or dilute our 50% interest in Casebia.

Non-Competition

During the term of the JV Agreement, neither we nor Bayer HealthCare, nor any of our respective affiliates, may develop, commercialize or otherwise exploit any competing product utilizing the CRISPR/Cas technology in any of the Casebia Fields unless, in the case of CRISPR or one of our affiliates, a target is the subject of a pre-existing license or an approved third-party agreement, or certain other excluded targets. In addition, in the event either we, Bayer HealthCare or a third party license a product candidate from Casebia pursuant to the Option Agreement discussed below, the non-licensing party or parties to the JV Agreement will be prohibited from developing, commercializing or otherwise exploiting any product utilizing CRISPR/Cas technology to target the same target as that of the licensed product candidate in any of the fields covered by such Option Agreement, so long as the licensing party is clinically developing, commercializing or otherwise exploiting such licensed product candidate.

Furthermore, upon a termination by either party for specified breaches of the other party, the defaulting party will be prohibited from utilizing the CRISPR/Cas technology to develop, commercialize or otherwise exploit product candidates in the field of the terminating party which would be competitive with the terminating party, for a period of two years following such termination.

Termination

The JV Agreement can be terminated by Bayer HealthCare and us upon mutual written consent. Either party may terminate the JV Agreement in the event of specified breaches by the other party or in the event the other party becomes subject to specified bankruptcy, winding up or similar circumstances. Either party may also terminate upon a change of control of the other party, as defined in the JV Agreement. Bayer HealthCare also has the right to terminate in the event (i) we are not able to maintain the intellectual property rights licensed to Casebia pursuant to the CRISPR IP Contribution Agreement or (ii) we have not achieved preclinical proof of concept with a CRISPR/Cas9 product candidate in a specified period of time. The JV Agreement may also be terminated by either party if, subsequent to the time that Bayer HealthCare has funded its entire $300 million commitment, the Management Board is unable to approve and obtain sufficient funding, within the time specified in the JV Agreement, to continue Casebia's operations for the next 18 months.

Subject to certain exceptions, in the event of a termination, all Casebia owned patents, know-how and technology will be jointly owned by us and Bayer HealthCare, with the right to sublicense. Upon termination, subject to certain exceptions, Bayer HealthCare will receive an exclusive license to Casebia CRISPR/Cas technology for all non-human therapeutic uses in the Bayer Field and a non-exclusive license for human therapeutic uses. Upon such termination, we will receive an exclusive license to Casebia CRISPR/Cas technology in human therapeutic areas, other than in the Bayer Field, and a non-exclusive license for human therapeutic uses in the Bayer Field. Upon any termination, all rights licensed to Casebia pursuant to the CRISPR IP Contribution Agreement will terminate, except for any rights licensed to third parties or to a party who has exercised an option pursuant to the Option Agreement described below.

IP Contribution Agreement with Casebia

As part of our contribution to Casebia, in March 2016, we and certain of our affiliates entered into the CRISPR IP Contribution Agreement with Casebia. Pursuant to the CRISPR IP Contribution Agreement, we and certain of our affiliated entities granted Casebia an exclusive, worldwide, fully paid-up, royalty-free license, including the right to sublicense, to the use of our CRISPR/Cas technology to research, develop, produce, commercialize and sell products in the Casebia Fields. As partial consideration for the license, Casebia is required to pay us an aggregate amount of $35 million for a technology access fee, consisting of an upfront payment of $20 million, which was paid at the closing of the JV Agreement in March 2016, and another payment of $15 million when we obtain specified intellectual property rights relating to our CRISPR/Cas9 technology outside of the United States, which was paid in December 2016 upon the signing of the IMA. The CRISPR IP Contribution Agreement also contains license grants from Casebia to us to various forms of intellectual property developed or in-licensed by Casebia. The CRISPR IP Contribution Agreement will terminate simultaneously with the termination of the JV Agreement, subject to survival of certain licenses granted during the term, including licenses granted pursuant to an exercise of an option pursuant to the Option Agreement.

Option Agreement with Bayer

In connection with the Closing, in March 2016, we, Bayer HealthCare and Casebia entered into an Option Agreement. Pursuant to the Option Agreement, in the event the FDA accepts an IND submitted by Casebia for any product candidate it is developing, both we and Bayer HealthCare have the right to submit an offer to enter into a license with Casebia for the exclusive right to develop, manufacture and commercialize the product candidate in certain Casebia Fields. In addition, Casebia is allowed to receive and consider unsolicited third-party offers, and both we and Bayer HealthCare can require Casebia to seek third-party offers for the applicable product candidate. The Option Agreement sets forth the procedures the Management Board will follow when considering and voting on any offers as well as the considerations on how to value any offer.

Collaboration Agreement with Vertex

On October 26, 2015, we entered into a Strategic Collaboration, Option and License Agreement, or the Collaboration Agreement, with Vertex Pharmaceuticals, Incorporated and Vertex Pharmaceuticals (Europe) Limited, together, Vertex. Pursuant to the Collaboration Agreement, we agreed to provide technology and options to obtain licenses relating to our CRISPR/Cas technology to Vertex in exchange for a $75 million upfront payment. In connection with the Collaboration Agreement, Vertex also made a $30 million equity investment in us. Under the Collaboration Agreement, Vertex has the option to exclusively license treatments for up to six collaboration targets that emerge from the four-year research collaboration under certain of our platform and background intellectual property to develop, manufacture, commercialize, sell and use therapeutics directed to each such collaboration target. For any non-hemoglobinopathies targets in-licensed for development, Vertex will pay future development, regulatory and sales milestones of up to $420 million per target, as well as royalty payments in the single digits to low teens on future sales of a commercialized product candidate. The milestone and royalty payments are each subject to reduction under certain specified conditions set forth in the Collaboration Agreement. For these therapies, Vertex is solely responsible for all research, development, manufacturing and global commercialization activities. Matters relating to hemoglobinopathies targets our governed by the JDA we have with Vertex, as summarized below

The initial focus of the Vertex collaboration will be to use CRISPR/Cas9 technology to discover and develop gene-based treatments for hemoglobinopathies and cystic fibrosis. Further discovery efforts focused on a specified number of other genetic targets will also be conducted under the Collaboration Agreement. We will be responsible for discovery activities, and the related expenses will be fully funded by Vertex. Under the Collaboration Agreement, we and Vertex have each agreed to certain exclusivity obligations with respect to targets subject to the Collaboration Agreement.

Either party can terminate the Collaboration Agreement upon the other party’s material breach, subject to specified notice and cure provisions. Vertex also has the right to terminate the Collaboration Agreement for convenience at any time upon 90 days’ written notice prior to any product receiving marketing approval and upon 270 days’ notice after a product has received marketing approval. In the event we and Vertex make a filing under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, for a collaboration target and such filing is not cleared within a specified time after such filing, the Collaboration Agreement will terminate with respect to that target. We may also terminate the Collaboration Agreement in the event Vertex challenges any of our patent rights.

Absent early termination, the Collaboration Agreement will continue until the expiration of the Vertex’s payment obligations under the Collaboration Agreement. Upon termination, the targets that are not licensed by Vertex will be returned to us.

In connection with entering into the JDA on December 12, 2017, we and Vertex entered into Amendment No. 1 to the Collaboration Agreement, or the Amendment. The Amendment, among other things, modified certain definitions and provisions of the Collaboration Agreement to make them consistent with the JDA and clarified how many options are exercised (or deemed exercised) in connection with certain targets specified under the Collaboration Agreement. The Amendment also amended other provisions of the Collaboration Agreement, including the expiration terms of the Collaboration Agreement.

Joint Development Agreement with Vertex

On December 12, 2017, we entered into the JDA with Vertex. The initial focus of the JDA is for the development of CTX001 for beta-thalassemia and SCD. In connection with entering into the JDA, we received a $7.0 million up-front payment from Vertex and are eligible for a one-time low seven-digit milestone payment upon the dosing of the second patient in a clinical trial with the initial product candidate. The net profits and net losses, as applicable, incurred under the JDA will be shared equally between us and Vertex.

The JDA includes, among other things, provisions relating to the following:

Governance. CRISPR and Vertex will form the following committees: (i) a joint steering committee to provide high-level oversight and decision making regarding the activities covered by the JDA, (ii) a joint development committee to provide oversight and decision making-making regarding development activities, (iii) a joint commercialization committee to provide oversight and decision-making regarding commercialization activities and (iv) a joint manufacturing committee to provide oversight and decision-making regarding manufacturing activities. Each of the committees will contain an equal number of representatives from each of CRISPR and Vertex.

Commercialization. The JDA provides that we will be the responsible for commercialization activities in the United States and Vertex will be responsible for commercialization activities outside of the United States.

Termination. Either party can terminate the JDA upon the other party's material breach, subject to specified notice and cure provisions, or, in the case of Vertex, in the event that we become subject to specified bankruptcy, winding up or similar circumstances. Either party may terminate the JDA in the event the other party commences or participates in any action or proceeding challenging the validity or enforceability of any patent that is licensed to such challenging party pursuant to the JDA. Vertex also has the right to terminate the JDA for convenience at any time after giving prior written notice.

If circumstances arise pursuant to which a party would have the right to terminate the JDA on account of an uncured material breach, such party may elect to keep the JDA in effect and cause such breaching party to be treated as if it had exercised its opt-out rights with respect to the products associated with such uncured material breach (described below) and the royalties payable to the breaching party would be reduced by a specified percentage.

Opt-Out Rights. Either party may opt of out of the development of a product candidate under the JDA after predetermined points in the development of the product candidate, on a candidate-by-candidate basis. In the event of such opt-out, the party opting-out will no longer share in the net profits and net losses associated with such product candidate and, instead, the opting out party will be entitled to high single to mid- teen percentage royalties on the net sales of such product, if commercialized.

Manufacturing

We have entered into certain manufacturing and supply arrangements with third-party suppliers to support production of our product candidates and their components. We plan to continue to rely on qualified third-party organizations to produce or process bulk compounds, formulated compounds, viral vectors or engineered cells for IND-supporting activities and early stage clinical trials. We expect that commercial quantities of any compound, vector, or engineered cells that we may seek to develop will be manufactured in facilities and by processes that comply with FDA and other regulations. At the appropriate time in the product development process, we will determine whether to establish manufacturing facilities or continue to rely on third parties to manufacture commercial quantities of any products that we may successfully develop. 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.

Competition

The biotechnology and pharmaceutical industries, including in the gene therapy and gene editing fields, are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on intellectual property and proprietary products. While we believe that our technology, development experience, and scientific knowledge provide us with competitive advantages, we currently face, and will continue to face, competition from many different sources, including major pharmaceutical, specialty pharmaceutical, and biotechnology companies, academic institutions and governmental agencies, and public and private research institutions. For any products that we may ultimately commercialize, not only will we compete with any existing therapies and those therapies currently in development, we will have to compete with new therapies that may become available in the future.

We compete in the segments of the pharmaceutical, biotechnology, and other related markets that utilize technologies encompassing genomic medicines to create therapies, including gene 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 on the development of therapies using CRISPR/Cas9 technology. Other companies developing CRISPR/Cas9 technology include Intellia and Editas Medicine, Inc.

There are additional companies developing therapies using additional gene-editing technologies, including TALENs, meganucleases, and zinc finger nucleases. The companies developing these additional gene-editing technologies include bluebird bio, Cellectis, Poseida Therapeutics, Precision Biosciences, and Sangamo Biosciences. Additional companies developing gene therapy products include Abeona Therapeutics, Avalanche Biotechnologies, Dimension Therapeutics, REGENXBIO, Spark Therapeutics and uniQure. In addition to competition from other gene-editing therapies or gene therapies, any products that we develop may also face competition from other types of therapies, such as small molecule, antibody, or protein therapies.

We may also face future competition from newly discovered gene editing technologies or new CRISPR-associated nucleases. While we believe that CRISPR/Cas9 will be highly effective for many therapeutic applications and are actively working to further enhance the technology, more efficient gene editing technologies may emerge. For example, recent publications by Feng Zhang, Ph.D., one of the founders of Editas Medicine, Inc. and others have elucidated a different CRISPR-associated nuclease, Cpf1, which can also edit human DNA. Some have argued that Cpf1 is superior to Cas9 for certain applications. Gene editing is a highly active field of research and new technologies, related or unrelated to CRISPR, may be discovered and create new competition.

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

In addition, due to the intense research and development that is taking place by several companies, including us and our competitors, in the gene editing field, the intellectual property landscape is in flux and highly competitive. There may be significant intellectual property related litigation and proceedings, in addition to the ongoing interference proceedings, relating to our owned and in-licensed, and other third party, intellectual property and proprietary rights in the future.

For example, in January 2016, at our request, the USPTO declared an interference between one of the pending U.S. patent applications we licensed from Dr. Emmanuelle Charpentier and twelve issued U.S. patents, and subsequently added one U.S. patent application, owned jointly by Broad. Because our application was filed first, the USPTO designated Dr. Charpentier, California and Vienna, or Vienna, collectively as “Senior Party” and designated Broad as “Junior Party.” Following motions by the parties and other procedural matters, the PTAB concluded in February 2017 that the declared interference should be dismissed because the claim sets of the two parties were not directed to the same patentable invention in accordance with the PTAB's two-way test for patent interferences. In particular, the Junior Party's claims in the interference were all limited to uses in eukaryotic cells, while the Senior Party's claims in the interference were not limited to uses in eukaryotic cells but included uses in all settings. Senior Party has appealed the decision to the U.S. Court of Appeals for the Federal Circuit. In parallel, either party can also pursue existing or new patent applications in the U.S. and elsewhere. Going forward, either party as well as other parties could seek a new interference related to the uses of the technology in eukaryotic cells or other aspects of the technology, and any existing or new patents could be the subject of other challenges to their validity of enforceability. In the context of a second interference or in other proceedings, a determination could be reached regarding that the Senior Party was not the first to invent, or it could be concluded that the contested subject matter is not patentable to the Senior Party and is patentable to the Junior Party, which in this case could preclude our U.S. patent applications from issuing as patents, in which case the proceedings would result in our losing the right to protect core innovations and our freedom to practice our core gene editing technology. If there is a second interference, either party could again appeal an adverse decision to the U.S. Court of Appeals for the Federal Circuit. In any case, it may be years before there is a final determination on priority. For example, Toolgen Inc., or Toolgen, filed Suggestions of Interference in the USPTO on April 13, 2015 and December 3, 2015, suggesting that they believe some of the claims in pending U.S. applications owned by Toolgen (U.S. Serial No. 14/685,568 and U.S. Serial No. 14/685,510, respectively) interfere with certain claims in five of the Broad patents currently involved in the interference with Dr. Emmanuelle Charpentier, California and Vienna. We are also aware of additional third parties that have pending patent applications relating to CRISPR technologies, which similarly may lead to further interference proceedings. For example, Rockefeller University has filed a continuation application (U.S. Serial No. 14/324,960) of an application filed by the Broad that Rockefeller's employee Luciano Marraffini as co-inventor of CRISPR/Cas9 technology; Vilnius University has filed applications in the United States and in other jurisdictions (published internationally as WO2013/141680 and WO2013/142578), Harvard University has filed applications in the United States and in other jurisdictions (published internationally as WO2014/099744), and Sigma-Aldrich has filed applications in the United States and in other jurisdictions (published internationally as WO2014/089290), each claiming aspects of CRISPR/Cas9 technology based on applications claiming priority to provisional filings in 2012. Numerous other filings are based on provisional applications filed after 2012.

Broad, Toolgen and Sigma have filed international counterparts of their U.S. applications, some of which were granted in Europe and/or other jurisdictions. We and third parties have initiated opposition proceedings against some of these grants, and we may in the future oppose other grants to these or other applicants. Similarly, if we should obtain patent grants in the U.S., Europe and other jurisdictions, these could also be the subject of oppositions or other post-grant procedures sought by third parties in order to revoke the grants or narrow the scope of granted claims. For example, our first patent granted in Europe has been opposed by multiple parties. Going forward, with existing and new challenges being filed against CRISPR/Cas9 cases in the U.S., Europe and elsewhere, and considering the number of interested parties, it is reasonable to expect that patents directed to the underlying technology will continue to be the subject of ongoing disputes over at least the next several years, and potentially beyond as decisions in favor or against particular parties may be the subject of appeals.

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, 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. Some jurisdictions outside of the United States also regulate the pricing of such products. The processes for obtaining marketing approvals in the United States and in other countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Licensure and Regulation of Biologics in the United States

In the United States, our candidate products would be regulated as biological products, or biologics, under the Public Health Service Act, or PHSA, and the Federal Food, Drug, and Cosmetic Act, or FDCA, and their implementing regulations. The failure to comply with the applicable U.S. requirements at any time during the product development process, including nonclinical testing, clinical testing, the approval process or post-approval process, may subject an applicant to delays in the conduct of a 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, untitled or warning letters, adverse publicity, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, and civil or criminal investigations and penalties brought by the FDA or the Department of Justice, or DOJ, or other governmental entities.

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

- preclinical laboratory tests, animal studies and formulation studies all performed in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated, or by a central IRB if appropriate;
- 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 the FDA's Good Clinical Practice, or GCP, regulations;
- preparation and submission to the FDA of a Biologics License Application, or BLA, for a biologic product requesting marketing for one or more proposed indications, including submission of detailed information on the manufacture and composition of the product and proposed labeling;
- 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 cGMP requirements and to assure that the facilities, methods, and controls are adequate to preserve the product's identity, strength, quality, and purity, and, if applicable, the FDA's current good tissue practice, or CGTP, for the use of human cellular and tissue products;
- satisfactory completion of any FDA audits of the nonclinical study and clinical trial sites to assure compliance with GLPs and GCPs, respectively, and the integrity of clinical data in support of the BLA;
- payment of user fees and securing FDA approval of the BLA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, adverse event reporting, and compliance with 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 animals. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA imposes a clinical hold based on concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research subjects would be exposed to unreasonable and significant 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 conduct of the IND study, including safety concerns or concerns due to non-compliance, it may impose a partial or complete clinical hold. This order issued by the FDA would delay either a proposed clinical study or cause suspension of an ongoing study, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigations may proceed or recommence but only under terms authorized by the FDA. This could cause significant delays or difficulties in completing planned clinical studies in a timely manner.

With gene therapy protocols, if the FDA allows the IND to proceed, but the Recombinant DNA Advisory Committee, or RAC, of the National Institute of Health, or NIH, decides that full public review of the protocol is warranted, the FDA will request at the completion of its IND review that sponsors delay initiation of the protocol until after completion of the RAC review process.

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 subsequent protocol amendments must be submitted to the FDA as part of the IND.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a non-U.S. clinical trial is not conducted under an IND, the sponsor may submit data from a well-designed and well-conducted clinical trial to the FDA in support of the BLA so long as the clinical trial is conducted in compliance with international guidelines for the ethical conduct of clinical research known as good clinical practice, or GCP, and the FDA is able to validate the data from the study through an onsite inspection if the FDA deems it necessary.

Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, subject informed consent, ethical factors, and the safety of human subjects. An IRB must operate in compliance with FDA regulations. The FDA or the clinical trial sponsor may suspend or terminate 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. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. 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 established under the 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 costlier Phase 3 clinical trials.
- ***Phase 3*** clinical trials are undertaken within an expanded patient population to further evaluate dosage and gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling.

Progress reports detailing the results, if known, of the clinical trials must be submitted at least annually to the FDA. Written IND safety reports must be submitted to the FDA and the investigators within 15 calendar days after determining that the information qualifies for reporting. IND safety reports are required for serious and unexpected suspected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk to humans exposed to the drug, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Additionally, a sponsor must notify FDA within 7 calendar days after receiving information concerning any unexpected fatal or life-threatening suspected adverse reaction.

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. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

Special Regulations and Guidance Governing Gene Therapy Products

It is possible that the procedures and standards applied to gene therapy products and cell therapy products may be applied to any CRISPR/Cas9 product candidates we may develop, but that remains uncertain at this point. The FDA has defined a gene therapy product as one that mediates its effects by transcription and/or translation of transferred genetic material and/or by integrating into the host genome and which are administered as nucleic acids, viruses, or genetically engineered microorganisms. The products may be used to modify cells *in vivo* or transferred to cells *ex vivo* prior to administration to the recipient. Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. Within the CBER, the review of gene therapy and related products is consolidated in the Office of Tissues and Advanced 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.

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

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

Compliance with cGMP and CGTP 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 CGTP. These requirements are found in FDA regulations that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue-based products, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the CGTP 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 for products intended for the U.S. market, and with analogous health regulatory agencies for products intended for other markets globally. Both U.S. and non-U.S. manufacturing establishments must register and provide additional information to the FDA and/or other health regulatory agencies upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether U.S. or non-U.S., is deemed misbranded under the FDCA, and could be affected by similar as well as additional compliance issues in other jurisdictions. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMP's and other laws. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA or other governing health regulatory agency 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 a license to market the product. The BLA must contain extensive manufacturing information and detailed information on the composition of the product and proposed labeling as well as payment of a user fee.

The FDA has 60 days after submission of the application to conduct an initial review to determine whether it is sufficient to accept for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or 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 through the submission of a major amendment 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 nonclinical study and clinical trial sites to assure compliance with GLPs and GCPs, respectively, 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, or ETASU. ETASU can include, but are not limited to, specific or 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, certain manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Fast Track, Breakthrough Therapy and Priority Review Designations

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

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

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the 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 adverse reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Accelerated Approval Pathway

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

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints but has indicated that such endpoints generally could support accelerated approval where a study demonstrates a relatively short-term clinical benefit in a chronic disease setting in which assessing durability of the clinical benefit is essential for traditional approval, but the short-term benefit is considered reasonably likely to predict long-term benefit.

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 has 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 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, untitled or 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 licensed and approved products that are placed on the market. Pharmaceutical products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Orphan Drug Designation

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

Orphan drug designation qualifies a company for tax credits and market exclusivity for seven years following the date of the product’s marketing approval if granted by the FDA. An application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. A product becomes an orphan when it receives orphan drug designation from the Office of Orphan Products Development, or OOPD, at the FDA based on acceptable confidential requests made under the regulatory provisions. The product must then go through the review and approval process for commercial distribution like any other product.

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

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

Pediatric Studies and Exclusivity

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

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

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

Biosimilars and Exclusivity

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

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 an IND and the submission date of a marketing application, plus the time between the submission date of the marketing application and the ultimate approval date, less any time the applicant failed to act with due diligence. 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.

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 health 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, or EU, 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 European Medicines Agency, or EMA, or the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by the EMA or these authorities before the product can be marketed and sold in the EU.

Clinical Trial Approval

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Commission Directive 2005/28/EC on GCP, a system for the approval of clinical trials in the EU has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of an EU 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 ethics committee has issued a favorable opinion. The CTA must be accompanied by an investigational medicinal product dossier with supporting information prescribed by Directive 2001/20/EC and Commission Directive 2005/28/EC and corresponding national laws of the member states and further detailed in applicable guidance documents.

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

Marketing Authorization

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

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products 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 (EC) No 1394/2007 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 (EC) No 1394/2007 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 Committee for Medicinal Products for Human Use, or 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 nine 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 EU'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 EU, 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 advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union under Directive 2001/83/EC, 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 (i) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (ii) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU 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 EU 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 ability to apply for a centralized EU marketing authorization. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, neither the European Commission nor 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.

For other markets in which we might in future seek to obtain marketing approval for the commercialization of products, there are other health regulatory regimes for seeking approval, and we would need to ensure ongoing compliance with applicable health regulatory procedures and standards, as well as other governing laws and regulations for each applicable jurisdiction.

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 various federal, state and/or local governments, as well as other payors, within the U.S. and in other countries globally, and the prices of pharmaceuticals have been a focus in these efforts. Governments and other payors 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, or HTAs) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. E.U. 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, or receiving 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 U.S. 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 be made or used a false record or statement to avoid, decrease, or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the U.S. False Claims Act;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal Health Insurance Portability and Accountability Act, or HIPAA, as amended by the U.S. 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 with respect to safeguarding the privacy, security, and transmission of individually identifiable information that constitutes protected health information, including mandatory contractual terms and restrictions on the use and/or disclosure of such information without proper authorization;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the U.S. Patient Protection and Affordable Care Act, as amended by the U.S. Health Care and Education Reconciliation Act, collectively the Affordable Care Act or ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, and requires certain manufacturers and applicable group purchasing organizations to report ownership and investment interests held by physicians or their immediate family members; and
- analogous laws and regulations in other national jurisdictions and states, 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 and other 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 other 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 ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the ACA 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 products, 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," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable products to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient products to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products. However, the IPAB implementation has been not been clearly defined. The ACA 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 ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers, and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

On January 20, 2017, United States President Donald Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress could consider subsequent legislation to replace elements of the Affordable Care Act that are repealed. It is unclear whether new legislation modifying the Affordable Care Act will be enacted, and, if so, precisely what the new legislation will provide, when it will be enacted and what impact it will have on the availability of healthcare and containing or lowering the cost of healthcare. We plan to continue to evaluate the effect that the Affordable Care Act and its possible repeal and replacement may have on our business.

There have been, and likely will continue to be, legislative and regulatory proposals at the national level in the U.S. and other jurisdictions globally, as well as at some regional, state and/or local levels within the U.S. or other jurisdictions, 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.

Employees

As of December 31, 2017 we had 127 full-time employees, 57 of whom held Ph.D. or M.D. degrees, 101 of whom were engaged in research and development, and 26 of whom were engaged in business development, finance, information systems, facilities, human resources, legal functions, or administrative support. None of our employees is represented by a labor union, and none of our employees has entered into a collective bargaining agreement with us. We consider our employee relations to be good.

Information Available on the Internet

From time to time, we may use our website to distribute material information. Our financial and other material information is routinely posted to and accessible on the Investors section of our website, available at www.crisprtx.com. Investors are encouraged to review the Investors section of our website because we may post material information on that site that is not otherwise disseminated by us. Information that is contained in and can be accessed through our website is not incorporated into, and does not form a part of, this Annual Report.

Item 1A. Risk Factors.

This report contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed in this report. Factors that could cause or contribute to these differences include, but are not limited to, those discussed below and elsewhere in this report and in any documents incorporated in this report by reference.

You should carefully consider the following risk factors, together with all other information in this report, including our financial statements and notes thereto, and in our other filings with the Securities and Exchange Commission. If any of the following risks, or other risks not presently known to us or that we currently believe to not be significant, develop into actual events, then our business, financial condition, results of operations or prospects could be materially adversely affected. If that happens, the market price of our common shares could decline, and shareholders may lose all or part of their investment.

Risks Related to Our Financial Position and Need for Additional Capital

We Have Incurred Significant Operating Losses Since Our Inception And Anticipate That We Will Incur Continued Losses For The Foreseeable Future.

We have funded our operations to date through proceeds from our initial public offering, or the IPO, and concurrent private placement of our common shares, private placements of our preferred shares and convertible securities and payments received from Casebia Therapeutics, LLP pursuant to our joint venture with Bayer HealthCare LLC, or Bayer Healthcare, and our Collaboration Agreement and Joint Development and Commercialization Agreement, or JDA, with Vertex Pharmaceuticals, Incorporated, or Vertex. Since inception, we have incurred significant operating losses. Our net loss was $68.4 million, $23.2 million, and $25.8 million for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017 and 2016, we had an accumulated deficit of $125.4 million and $57.1 million, respectively. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our shareholders' deficit and working capital. We anticipate that our expenses will increase substantially if and as we:

- initiate clinical trials for our lead hemoglobinopathy program, CTX001, targeting beta-thalassemia and sickle cell disease
- continue our current research programs and our preclinical and clinical development of product candidates;
- seek to identify additional research programs and additional product candidates;
- conduct Investigational New Drug, or IND, supporting preclinical studies and initiate clinical trials for our most advanced product candidates which are from our hemoglobinopathy program targeting beta-thalassemia and sickle cell disease;
- initiate preclinical studies and clinical trials for any other product candidates we identify and choose to develop;
- maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals for any of our product candidates that successfully complete clinical trials;
- further develop our gene editing technology;
- hire additional clinical, quality control and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product candidate development;
- acquire or in-license other technologies;
- ultimately establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain marketing approval; and
- operate as a public company.

As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing gene editing product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

We Will Need To Raise Substantial Additional Funding, Which Will Dilute Our Shareholders. If We Are Unable To Raise Capital When Needed, We Would Be Forced To Delay, Reduce Or Eliminate Some Of Our Product Development Programs Or Commercialization Efforts.

The development of gene editing product candidates is capital intensive. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate preclinical studies and clinical trials for and seek marketing approval for our product candidates. In addition, if we obtain marketing approval for any of our product candidates, 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 Bayer Healthcare or Vertex, or other future collaborators. We may also need to raise additional funds sooner if we choose to pursue additional indications or geographies for our product candidates or otherwise expand more rapidly than we presently anticipate. In addition, relative to prior years when we were a private company, we expect to incur significant additional 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 certain of our research and development programs or future commercialization efforts.

As of December 31, 2017 and 2016, we had cash of approximately $239.8 million and $315.5 million, respectively. In January 2018, the Company completed an offering of 5,750,000 shares of common, which were sold at a price of $22.75 per share. This offering resulted in $122.6 million of net proceeds to the Company. The underwriting discount of $7.8 million and other expenses of $0.4 million related to the equity offering were recorded as an offset to additional paid-in capital. With our cash on hand as of December 31, 2017 and the proceeds from the January 2018 offering, we expect cash and cash equivalents to be sufficient to fund its current operating plan through at least the next 24 months.

Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- the scope, progress, results and costs of clinical trials, drug discovery, preclinical development, and laboratory testing for our wholly owned and partnered product candidates;
- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of establishing and maintaining a supply chain for the development and manufacture of our product candidates;
- the success of our current joint venture with Bayer Healthcare and our collaboration with Vertex;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we obtain;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the costs of fulfilling our obligations under the Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement to reimburse other parties for costs incurred in connection with the prosecution and maintenance of associated patent rights;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of establishing or contracting for manufacturing capabilities if we obtain regulatory approvals to manufacture our product candidates;
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market our product candidates; and
- our ability to establish and maintain healthcare coverage and adequate reimbursement.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our shareholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our shareholders and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

We Have A Limited Operating History, Which May Make It Difficult To Evaluate Our Technology And Product Development Capabilities And Predict Our Future Performance.

We are early in our development efforts and we have not initiated clinical trials for any of our product candidates. We were formed in October 2013, have no products approved for commercial sale and have not generated any revenue from product sales. Our ability to generate product revenue or profits, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. We may never be able to develop or commercialize a marketable product.

We have submitted clinical trial applications, or CTAs, in various European jurisdictions for a clinical trial in beta-thalassemia for our lead product candidate from our hemoglobinopathy program and intend to file an IND with the United Stated Food and Drug Administration, or FDA for our hemoglobinopathy program targeting sickle cell disease in the first half of 2018, but have not yet commenced clinical trials for such programs. Each of our other programs requires additional discovery research and then preclinical development. All of our programs, including our hemoglobinopathy program, require clinical development, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. In addition, our product candidates must be approved for marketing by the FDA or certain other health regulatory agencies, including the European Medicines Agency, or EMA, before we may commercialize any product.

Our limited operating history, particularly in light of the rapidly evolving gene editing field, may make it difficult to evaluate our technology and industry and predict our future performance. Our short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer. Similarly, we expect that our financial condition and operating results will fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. As a result, our shareholders should not rely upon the results of any quarterly or annual period as an indicator of future operating performance.

In addition, as an early stage company, we have encountered unforeseen expenses, difficulties, complications, delays and other known and unknown circumstances. As we advance our product candidates, we will need to transition from a company with a research focus to a company capable of supporting clinical development and if successful, commercial activities. We may not be successful in such a transition.

Our Ability To Use Tax Loss Carryforwards In Switzerland May Be Limited.

Under Swiss law, we are entitled to carry forward losses we incur for a period of seven years and we can offset future profits, if any, against such losses. As of December 31, 2017, we reported tax loss carry forwards from inception through 2017 for purposes of Swiss federal direct taxes in the aggregate amount of CHF 103.1 million (including the loss incurred in 2017). As we have moved our legal seat from the Canton of Basel-Stadt to the Canton of Zug mid of 2017, it will be the Canton of Zug, which is in charge for assessing our tax return including our carry forward losses (to be noted that there will be a pro-rata allocation between the Canton of Basel-Stadt and Zug for capital tax purposes in 2017). No ruling regarding taxation as a mixed company has been filed with the Zug tax authorities; however, based on the practice of the Canton of Zug, we can apply for taxation as a mixed company in the tax return as long as the respective law is in force and we fulfill the respective criteria. According to the practice of the Canton of Zug and deviating from the tax rules of the Canton of Basel-Stadt a mixed company profit allocation is only performed once the company is profit making. Therefore, the tax loss carry forwards at cantonal level are the same as at federal level and therefore amount to some CHF 103.1 million in aggregate as of December 31. 2017. It is to be noted in this regard that tax losses are only finally assessed by the tax authorities when offset with taxable profit (which will not be the case as long we are loss making). If not used, these tax losses will expire seven years after the year in which they occurred. Due to our limited income, there is a high risk that the tax loss carry forwards will expire partly or entirely. For 2017, the tax return has – in accordance with Swiss tax law – not yet been filed. Therefore, for 2017 the loss carried forward will only be claimed with filing of the tax return for the tax year 2017.

Risks Related to Our Business, Technology and Industry

We Are Early In Our Development Efforts And We Have Not Initiated Clinical Trials For Any Of Our Product Candidates. It Will Be Many Years Before We Or Our Collaborators Commercialize A Product Candidate, If Ever. If We Are Unable To Advance Our Product Candidates To Clinical Development, Obtain Regulatory Approval And Ultimately Commercialize Our Product Candidates, Or Experience Significant Delays In Doing So, Our Business Will Be Materially Harmed.

We are early in our development efforts and have focused our research and development efforts to date CRISPR/Cas9, gene editing technology, identifying our initial targeted disease indications and our initial product candidates. Our future success depends heavily on the successful development of our CRISPR/Cas9 gene editing product candidates including our most advanced product candidate, CTX001, which targets beta-thalassemia and sickle cell disease. We have invested substantially all of our efforts and financial resources in the identification and preclinical development of our current product candidates. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. For example, our research programs, including those subject to our joint venture with Bayer Healthcare and Collaboration Agreement and the Joint Development and Commercialization Agreement, or the JDA, with Vertex, may fail to identify potential product candidates for clinical development for a number of reasons or may fail to successfully advance any product candidates through clinical development. 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. We currently generate no revenue from sales of any product and we may never be able to develop or commercialize a marketable product.

In December 2017, we submitted CTAs in various European jurisdictions for CTX001 to begin our first clinical trial in beta-thalassemia and plan, following a pre-IND meeting with the FDA, to file an IND with the FDA in the first half of 2018 to begin our first clinical trial for CTX001 in sickle cell disease. The filing of future CTAs or INDs for any other product candidate we develop is subject to the identification and selection of guide RNA with acceptable efficiency. Subject to successful completion of preclinical toxicology testing, we also intend to file an IND for CTX101 by the end of 2018. Commencing any of our clinical trials is also subject to acceptance by the European regulatory authorities of our CTAs, or the FDA of our INDs, and finalizing the trial design based on discussions with the applicable regulatory authorities, including the Recombinant DNA Advisory Committee, or RAC, of the U.S. National Institutes of Health, or NIH. In the event that the European regulatory authorities, FDA or RAC requires us to complete additional preclinical studies or we are required to satisfy other requests, the start of our first clinical trial for our hemoglobinopathy programs or any of our other programs may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, they could disagree that we have satisfied their requirements to commence our clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect.

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

The success of our product candidates will depend on several factors, including the following:

- successful completion of clinical trials and preclinical studies;
- sufficiency of our financial and other resources to complete the necessary clinical trials and preclinical studies;
- ability to develop safe and effective delivery mechanisms for our *in vivo* therapeutic programs;
- ability to identify optimal RNA sequences to guide genomic editing;
- entry into collaborations to further the development of our product candidates;
- a positive recommendation of the Recombinant DNA Advisory Committee of the NIH;
- approval of CTAs or INDs for our product candidates to commence clinical trials;

- successful enrollment in, and completion of, clinical trials and preclinical studies;
- successful data from our clinical program that supports an acceptable risk-benefit profile of our product candidates for the intended patient populations;
- receipt of regulatory and marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers for clinical supply and commercial manufacturing and, where applicable, commercial manufacturing capabilities;
- successful development of our internal manufacturing processes and transfer to larger-scale facilities operated by either a contract manufacturing organization, or CMO, or by us;
- establishment and maintenance of patent and trade secret protection or regulatory exclusivity for our product candidates;
- commercial launch of our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of the product candidates, if and when approved, by patients, the medical community and third-party payors;
- effective competition with other therapies and treatment options;
- establishment and maintenance of healthcare coverage and adequate reimbursement;
- enforcement and defense of intellectual property rights and claims;
- maintenance of a continued acceptable safety profile of the product candidates following approval; and
- achieving desirable medicinal properties for the intended indications.

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

- regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future; to date, no products that involve the genetic modification of patient cells have been approved in the United States and only one gene therapy product has been approved in the European Union;
- improper insertion of a gene sequence into a patient’s chromosome could lead to lymphoma, leukemia or other cancers, or other aberrantly functioning cells; and
- the FDA recommends a follow-up observation period of 15 years or longer for all patients who receive treatment using gene therapies, and we may need to adopt and support such an observation period for our product candidates.

If we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

Our CRISPR/Cas9 Gene Editing Product Candidates Are Based On A New Gene Editing Technology, Which Makes It Difficult To Predict The Time And Cost Of Development And Of Subsequently Obtaining Regulatory Approval, If At All. There Have Only Been A Limited Number Of Clinical Trials Of Product Candidates Based On Gene Editing Technology And No Gene Editing Products Have Been Approved In The United States Or In The European Union.

CRISPR/Cas9 gene editing technology is relatively new, and no products based on CRISPR/Cas9 or other similar gene editing technologies have been approved in the United States or the European Union and only a limited number of clinical trials of products based on gene editing technologies have been commenced. As such it is difficult to accurately predict the developmental challenges we may incur for our product candidates as they proceed through product discovery or identification, preclinical studies and clinical trials. In addition, because we have not commenced clinical trials, we have not yet been able to assess safety in humans, and there may be long-term effects from treatment with any product candidates that we develop 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, testing of our product candidates in animal models may not be predictive of the results we observe in human clinical trials of our product candidates for either safety or efficacy. Also, animal models may not exist for some of the diseases we choose 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 gene editing technology, or any similar or competitive gene editing technologies, will result in the identification, development, and regulatory approval of any products. There can be no assurance that any development problems we experience in the future related to our gene editing technology or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. 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.

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 product candidate. No products based on gene editing technologies have been approved by regulators. As a result, the regulatory approval process for product candidates such as ours is uncertain and may be more expensive and take longer than the approval process for product candidates based on other, better known or more extensively studied technologies. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or the European Union or how long it will take to commercialize our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product candidate to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects may be harmed.

The FDA, The NIH And The EMA Have Demonstrated Caution In Their Regulation Of Gene Therapy Treatments, And Ethical And Legal Concerns About Gene Therapy And Genetic Testing May Result In Additional Regulations Or Restrictions On The Development And Commercialization Of Our Product Candidates, Which May Be Difficult To Predict.

The FDA, NIH and the EMA have each expressed interest in further regulating biotechnology, including gene therapy and genetic testing. For example, the EMA advocates a risk-based approach to the development of a gene therapy product. Agencies at both the federal and state level in the United States, as well as the U.S. congressional committees and other governments or governing agencies, have also expressed interest in further regulating the biotechnology industry. Such action may delay or prevent commercialization of some or all of our product candidates. Within the broader genome product field, uniQure N.V.'s Glybera has received marketing authorization from the European Commission, and to date no gene therapy products have received marketing approval in the United States.

Regulatory requirements in the United States and in other jurisdictions governing gene therapy products have changed frequently and may continue to change in the future. The FDA established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research to consolidate the review of gene therapy and related products, and established the Cellular, Tissue and Gene Therapies Advisory Committee to advise this review. Prior to submitting an IND, our human clinical trials are subject to review by the NIH Office of Biotechnology Activities, or OBA, Recombinant DNA Advisory Committee, or the RAC. Following an initial review, RAC members make a recommendation as to whether the protocol raises important scientific, safety, medical, ethical or social issues that warrant in-depth discussion at the RAC's quarterly meetings. Even though the FDA decides whether individual gene therapy protocols may proceed under an IND, the RAC's recommendations are shared with the FDA and the RAC public review process, if undertaken, can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and has not objected to its initiation or has notified the sponsor that the study may begin. Conversely, the FDA can put an IND on a clinical hold even if the RAC has provided a favorable review or has recommended against an in-depth, public review. Moreover, under guidelines published by the NIH, patient enrollment in our future gene editing clinical trials cannot begin until the investigator for such clinical trial has received a letter from the OBA indicating that the RAC review process has been completed; and Institutional Biosafety Committee, or IBC, approval as well as all other applicable regulatory authorizations have been obtained. In addition to the government regulators, the IBC and institutional review board, or IRB, of each institution at which we conduct clinical trials of our product candidates, or a central IRB if appropriate, would need to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of any of our product candidates. Similarly, the EMA governs the development of gene therapies in the European Union and may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines. These regulatory review agencies and committees and the new requirements or 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 our product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory agencies and committees and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our or our collaborators' ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

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 undesirable side effects, unexpected characteristics or other serious adverse events, including off-target cuts of DNA, or the introduction of cuts in DNA at locations other than the target sequence. These 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. 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. Possible adverse side effects that could occur with treatment with gene editing products include an immunologic reaction after administration which could substantially limit the effectiveness of the treatment. Additionally, immunotherapy, and its method of action of harnessing the body's immune system, is powerful and could lead to serious side effects that we only discover in clinical trials. Unforeseen side effects could arise either during clinical development or, if such side effects are more rare, after our product candidates have been approved by regulatory authorities and the approved product has been marketed, resulting in the exposure of additional patients. If our CRISPR/Cas9 gene editing technology demonstrates a similar effect, we may decide or be required to halt or delay preclinical development or clinical development of our product candidates. 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, EMA or other comparable health regulatory authorities could order us to cease further clinical studies 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, or REMS, to ensure that the benefits of treatment with such product candidate outweighs the risks for each potential patient, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients, a communication plan to health care practitioners, extensive patient monitoring, or distribution systems and processes that are highly controlled, restrictive, and more costly than what is typical for the industry. Furthermore, if we or others later identify undesirable side effects caused by any product candidate that we to develop, several potentially significant negative consequences could result, including:

- regulatory authorities may revoke licenses or suspend, vary 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 our CRISPR/Cas9 technology and 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.

If We Experience Delays Or Difficulties In The Enrollment Of Patients In Clinical Trials, Our Receipt Of Necessary Regulatory Approvals Could Be Delayed Or Prevented.

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

Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- size of the patient population and process for identifying subjects;
- design of the trial protocol;
- availability and efficacy of approved medications for the disease under investigation;
- availability of genetic testing for potential patients;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- eligibility and exclusion criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial;
- perceived risks and benefits of gene editing and cellular therapies as therapeutic approaches;
- 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.

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.

Positive Results From Early Preclinical Studies Of Our Product Candidates Are Not Necessarily Predictive Of The Results Of Later Preclinical Studies And Any Future Clinical Trials Of Our Product Candidates. If We Cannot Replicate The Positive Results From Our Earlier Preclinical Studies Of Our Product Candidates In Our Later Preclinical Studies And Future Clinical Trials, We May Be Unable To Successfully Develop, Obtain Regulatory Approval For And Commercialize Our Product Candidates.

Any positive results from our preclinical studies of our product candidates may not necessarily be predictive of the results from required later preclinical studies and clinical trials. Similarly, even if we are able to complete our planned preclinical studies or any future clinical trials of our product candidates according to our current development timeline, the positive results from such preclinical studies and clinical trials of our product candidates may not be replicated in subsequent preclinical studies or clinical trial results.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical and other nonclinical findings made while clinical trials were underway or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical, nonclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or EMA approval.

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, by EMA in the European Union 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 or clearance to market any product candidates from regulatory authorities in any jurisdiction and it is possible that none of our product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval or clearance. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations, or CROs, or regulatory consultants 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, efficacy 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 in other jurisdictions, 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 are 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 product 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.

We May Never Obtain FDA Approval For Any Of Our Product Candidates In The United States, And Even If We Do, We May Never Obtain Approval For Or Commercialize Any Of Our Product Candidates In Any Other Jurisdiction, Which Would Limit Our Ability To Realize Their Full Market Potential.

In order to eventually market any of our product candidates in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a jurisdiction-by-jurisdiction basis regarding safety and efficacy. Approval by the FDA in the United States, if obtained, does not ensure approval by regulatory authorities in other countries or jurisdictions. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking regulatory approval in multiple jurisdictions could result in difficulties and costs for us and require additional preclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in certain countries. Regulatory approval processes outside the United States involve all of the risks associated with FDA approval. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be unrealized.

Gene Editing Products Are Novel And May Be Complex And Difficult To Manufacture. We Could Experience Manufacturing Problems That Result In Delays In The Development Or Commercialization Of Our Product Candidates Or Otherwise Harm Our Business.

The manufacturing process used to produce CRISPR/Cas9-based product candidates may be complex, as they are novel and have not been validated for clinical and commercial production. Several factors could cause production interruptions, including equipment malfunctions, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error or disruptions in the operations of our suppliers.

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

In addition, the FDA, the EMA and other health 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 health regulatory authorities may require that we not distribute a lot until the relevant agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects. Problems in our manufacturing process could restrict our ability to meet market demand for our products.

We also may encounter problems hiring and retaining directly or through contract manufacturing organizations the experienced scientific, quality-control and manufacturing personnel needed to operate our manufacturing processes, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements. Any problems in our manufacturing process or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs.

Adverse Public Perception Of Gene Editing And Cellular Therapy Products May Negatively Impact Demand For, Or Regulatory Approval Of, Our Product Candidates.

Our product candidates involve editing the human genome. The clinical and commercial success of our product candidates will depend in part on public acceptance of the use of gene editing therapies for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene editing is unsafe, unethical, or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Negative public reaction to gene therapy in general could result in greater government regulation and stricter labeling requirements of gene editing products, including any of our product candidates, and could cause a decrease in the demand for any products we may develop. 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 particular, gene editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns relating to the application of gene editing technology to human embryos or the human germline. For example, in April 2016, Chinese scientists reported on their attempts to edit the genome of human embryos to modify the gene for hemoglobin beta. This is the gene in which a mutation occurs in patients with the inherited blood disorder beta-thalassemia. Although this research was purposefully conducted in embryos that were not viable, the work prompted calls for a moratorium or other types of restrictions on gene editing of human eggs, sperm, and embryos. The Alliance for Regenerative Medicine in Washington, D.C. has called for a voluntary moratorium on the use of gene editing technologies, including CRISPR/Cas9, in research that involves altering human embryos or human germline cells. Similarly, the NIH has announced that it would not fund any use of gene 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. Research on embryos is more tightly controlled in many other European countries.

Although we do not use our technologies to edit human embryos or the human germline, such public debate about the use of gene 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 gene 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.

If, In The Future, We Are Unable To Establish Sales And Marketing Capabilities Or Enter Into Agreements With Third Parties To Sell And Market Products Based On Our Technologies, We May Not Be Successful In Commercializing Our Products If And When Any Products Candidates Are Approved And We May Not Be Able To Generate Any Revenue.

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

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

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

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

- the lack of complementary treatments to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

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

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 product, 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, current Good Manufacturing Practice, or cGMP, requirements relating to quality control, quality assurance and corresponding maintenance of records and documents and requirements regarding 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 product 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 product. The FDA also may place other conditions on approvals including the requirement for a REMS to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the Biologics License Application, or BLA, must submit a proposed REMS before it can obtain approval. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

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 Products, When And If Any Of Them Are Approved.

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of biologics 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 products 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 United States Department of Justice. Violation of the Federal Food, Drug, 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 a product candidate, including adverse events of unanticipated severity or frequency, or with our manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on such products, manufacturers, or manufacturing processes;
- restrictions on the labeling or marketing of a product;

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

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

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 also inhibit our ability to commercialize any product candidates we may develop and adversely affect our business, financial condition, results of operations, and prospects.

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 gene therapy could result in additional regulations restricting or prohibiting our products. Even with the requisite approvals from FDA in the United States, the EMA in the European Union and other regulatory authorities internationally, the commercial success of our product candidates will depend, in significant part, on the acceptance of physicians, patients and health care payors of gene therapy products in general, and our product candidates in particular, as medically necessary, cost-effective and safe. Any product that we commercialize may not gain acceptance by physicians, patients, health care payors and others in the medical community. The degree of market acceptance of gene therapy products and, in particular, our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy, durability and safety of such product candidates as demonstrated in any future clinical trials;
- the potential and perceived advantages of product candidates over alternative treatments;
- the cost of treatment relative to alternative treatments;
- the clinical indications for which the product candidate is approved by FDA or the EMA;
- patient awareness of, and willingness to seek, genotyping;
- the willingness of physicians to prescribe new therapies;
- the willingness of the target patient population to try new therapies;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of 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 strength of marketing and distribution support;

- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party payor coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and future clinical trials, market acceptance of the product will not be fully known until after it is launched. If our product candidates do not achieve an adequate level of acceptance following regulatory approval, if ever, we may not generate significant product revenue and may not become profitable.

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.

We have limited financial and managerial resources. 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 timely capitalize on viable commercial products 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 products. 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.

We Face Significant Competition In An Environment Of Rapid Technological Change And The Possibility That Our Competitors May Achieve Regulatory Approval Before Us Or Develop Therapies That Are More Advanced Or Effective Than Ours, Which May Harm Our Business And Financial Condition, And Our Ability To Successfully Market Or Commercialize Our Product Candidates.

The biotechnology and pharmaceutical industries, including the gene therapy field, are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions, some or all of which may have greater access to capital or resources than we do.

We are aware of several companies focused on developing gene editing in various indications using CRISPR/Cas9 gene editing technology, including Intellia Therapeutics, Inc. and Editas Medicine, Inc., or Editas. There can be no certainty that other gene editing technologies will not be considered better or more attractive than our technology for the development of products. For example, Editas has exclusively licensed a CRISPR system involving a different protein, Cpf1, which can also edit human DNA as well as advanced forms of Cas9. Editas and certain of its scientific founders have asserted that Cpf1 may work better than Cas9 in some cases. Cas9 may be determined to be less attractive than Cpf1 or other CRISPR proteins that have yet to be discovered.

There are additional companies developing therapies using additional gene editing technologies, including transcription activator-like effector nucleases (TALENs), meganucleases and zinc finger nucleases (ZFNs). These companies include bluebird bio, Cellectis, Poseida Therapeutics, Precision Biosciences, and Sangamo Biosciences. Additional companies developing gene therapy products include Abeona Therapeutics, Avalanche Biotechnologies, Dimension Therapeutics, REGENXBIO, Spark Therapeutics and uniQure.

In addition to competition from other gene editing therapies or gene therapies, any product we may develop may also face competition from other types of therapies, such as small molecule, antibody or protein therapies. In addition, new scientific discoveries may cause CRISPR/Cas9 technology, or gene editing as a whole, to be considered an inferior form of therapy.

Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical studies, 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, have broader acceptance and higher rates of reimbursement by third party payors 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 and our patents may not be sufficient to prevent our competitors from commercializing competing 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.

To become and remain profitable, we must develop and eventually commercialize product candidates with significant market potential, which will require us to be successful in a range of challenging activities. These activities can include completing preclinical studies and clinical trials of our product candidates, obtaining marketing and reimbursement approval for these product candidates, manufacturing, marketing and selling those products that are approved and satisfying any post marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our Company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our Company also could cause shareholders to lose all or part of their investment.

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 biologic products vary widely from country to country. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some non-U.S. 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 product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product 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 products successfully also will depend in part on the extent to which reimbursement for these products 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 product 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 products, and reimbursement coverage may be more limited than the purposes for which the product is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any product 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 products, 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 product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. Net prices for products 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 products 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 products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

Risks Related to Our Relationships with Third Parties

If Conflicts Arise Between Us And Our Collaborators Or Strategic Partners, These Parties May Act In A Manner Adverse To Us And Could Limit Our Ability To Implement Our Strategies.

If conflicts arise between our corporate or academic collaborators or strategic partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Some of our academic collaborators and strategic partners are conducting multiple product development efforts within each area that is the subject of the collaboration with us. Our collaborators or strategic partners, however, may develop, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for our product candidates.

Some of our collaborators or strategic partners could also become our competitors in the future. Our collaborators or strategic partners could develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, or fail to devote sufficient resources to the development and commercialization of products. Any of these developments could harm our product development efforts.

Our Collaborators Or Strategic Partners May Decide To Adopt Alternative Technologies Or May Be Unable To Develop Commercially Viable Products With Our Technology, Which Would Negatively Impact Our Revenues And Our Strategy To Develop These Products.

Our collaborators or strategic partners may adopt alternative technologies, which could decrease the marketability of our CRISPR/Cas9 gene editing technology. Additionally, because our current are and we anticipate that any future collaborators or strategic partners will be working on more than one development project, they could choose to shift their resources to projects other than those they are working on with us. If they do so, this would delay our ability to test our technology and would delay or terminate the development of potential products based on our CRISPR/Cas9 gene editing technology. Further, our collaborators and strategic partners may elect not to develop products arising out of our collaborative and strategic partnering arrangements or to devote sufficient resources to the development, manufacturing, marketing or sale of these products. The failure to develop and commercialize a product candidate pursuant to our agreements with our current or future collaborators would prevent us from receiving future milestone and royalty payments which would negatively impact our revenues.

Our Collaborators And Strategic Partners May Control Aspects Of Our Clinical Trials and Commercialization Efforts, Which Could Result In Delays And Other Obstacles In The Commercialization Of Our Proposed Products And Materially Harm Our Results Of Operations.

For some programs, we will depend on third party collaborators and strategic partners to design and conduct our clinical trials, and for any approved products, the commercialization of such products. As a result, we may not be able to conduct these programs in the manner or on the time schedule we currently contemplate, which may negatively impact our business operations. In addition, if any of these collaborators or strategic partners withdraw support for our programs or proposed products or otherwise impair their development or commercialization, our business could be negatively affected. In October 2015, we entered into a four-year collaboration agreement with Vertex to research, develop and commercialize new treatments aimed at the underlying genetic causes of human diseases, including beta-thalassemia and sickle cell. In December 2017, we entered into the JDA with Vertex, initially for the development and commercialization of CTX001 for beta-thalassemia and sickle cell disease. In addition, in December 2015, we entered into an agreement with Bayer Healthcare to create a joint venture to discover and commercialize therapeutics for the treatment of blood disorders, blindness and heart disease in addition to select indications related to other sensory organs, metabolic diseases and autoimmune diseases based on our CRISPR/Cas9 gene editing technology.

We and Bayer Healthcare each hold a 50% interest in the joint venture and each have two designees on the management board. As such, we cannot control all aspects of the clinical development and commercialization of any product candidate developed by the joint venture. Similarly, under our collaboration agreement with Vertex, Vertex has sole authority to select genetic targets to pursue and we will not have control over the development of any product candidates for the selected genetic targets. Under the JDA, we and Vertex have an equal number of representatives on the various committees contemplated by the JDA, which will prevent us from having sole control of the development of CTX001 or any future product candidates subject to the JDA. Furthermore, pursuant to the JDA, Vertex will be solely responsible for the commercialization activities of any approved products subject to the JDA outside of the United States. Our lack of control over the clinical development and commercialization activities in our agreements with Bayer Healthcare and Vertex could cause delays or other difficulties in the development and commercialization of product candidates, which may prevent among other things, completion of intended IND filings for the first clinical trial for our hemoglobinopathy program targeting sickle cell disease in a timely fashion, if at all, or the completion or delay in BLA filings, as well as the timely initiation of clinical trials for beta-thalassemia upon approval of the CTA, if at all.

In addition, the termination of our agreements with Vertex would prevent us from receiving any milestone, royalty payments and other benefits under that agreement. The termination of our joint venture with Bayer Healthcare would prevent us from participating in the profits of the joint venture. Either occurrence would have a materially adverse effect on our results of operations.

We May Seek To Establish Additional Collaborations And, If We Are Not Able To Establish Them On Commercially Reasonable Terms, We May Have To Alter Our Development And Commercialization Plans.

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

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for any additional collaborations 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 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 drugs, 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 for our product candidate. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. For example, we have granted exclusive rights to Vertex for certain genetic targets, and during the term of the collaboration agreement, we will be restricted from granting rights to other parties to use our CRISPR/Cas9 technology to pursue therapies that address these genetic targets. Similarly, pursuant to our joint venture agreement with Bayer Healthcare, during the term of the joint venture, and for a specified period after the termination of the joint venture, we will be prohibited from developing products that use our CRISPR/Cas9 technology in specified fields that would compete with the joint venture and Bayer, respectively. The non-competition provisions in each of these agreements could limit our ability to enter into strategic collaborations with future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. 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. If we are unable to negotiate and enter into new collaborations, 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 our product candidates or bring them to market and generate product revenue.

We Expect To Rely On Third Parties To Conduct Our Clinical Trials And Certain Aspects Of Our Preclinical Studies For Our Product Candidates. If These Third Parties Do Not Successfully Carry Out Their Contractual Duties, Comply With Regulatory Requirements Or Meet Expected Deadlines, We May Not Be Able To Obtain Regulatory Approval For Or Commercialize Our Product Candidates And Our Business Could Be Substantially Harmed.

We expect to rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct future clinical trials and we currently rely on third parties to conduct certain aspects of our preclinical studies for our product candidates. Nevertheless, we are responsible for ensuring that each of our preclinical studies and any future clinical trials we sponsor are conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards and our reliance on CROs will not relieve us of our regulatory 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 regulations, commonly referred to as Good Clinical Practices, or GCPs, 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. For any violations of laws and regulations during the conduct of our preclinical studies and clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

We and our CROs will be required to comply with regulations, including GCPs, for conducting, monitoring, recording and reporting the results of preclinical studies and clinical trials to ensure that the data and results are scientifically credible and accurate and that the trial patients are adequately informed, among other things, of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by FDA, the Competent Authorities of the Member States of the European Economic Area and comparable health regulatory authorities for any drugs in clinical development. The FDA enforces GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and FDA or comparable health regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our future clinical trials will comply with GCPs. In addition, our future clinical trials must be conducted with product candidates produced in accordance with the requirements in cGMP regulations. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action.

Although we intend to design the clinical trials for our product candidates, CROs will conduct all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future preclinical studies and clinical trials will also result in less direct control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical studies and clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs do not perform preclinical studies and future clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our product candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our product candidates, or our development programs may be materially and irreversibly harmed. If we are unable to rely on preclinical and clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct and this could significantly delay commercialization and require significantly greater expenditures.

We Expect To Rely On Third Parties To Manufacture Our Clinical Product Supplies, And We Intend To Rely On Third Parties For At Least A Portion Of The Manufacturing Process Of Our Product Candidates, If Approved. Our Business Could Be Harmed If The Third Parties Fail To Provide Us With Sufficient Quantities Of Product Inputs Or Fail To Do So At Acceptable Quality Levels Or Prices.

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

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

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, Exclusion From Government Healthcare Programs, Contractual Damages, Reputational Harm And Diminished Profits And Future Earnings.

Although we do not currently have any drugs on the market, once we begin commercializing our product candidates, if ever, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the U.S. federal government and states as well as other national, regional or local governments in other jurisdictions in which we conduct our business.

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 product candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal 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 a state or Federal healthcare program, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violation of the statute may give rise to criminal and/or civil penalties;
- the federal civil and criminal false claims laws, including the civil False Claims Act, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, 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, fictitious or fraudulent or knowingly making, using or causing to be made or used a false record or 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. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false of fraudulent claim for purposes of the False Claims Act;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as further amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations which impose certain requirements on covered entities, including healthcare providers, health plans and healthcare clearing houses, as well as their business associates that perform certain services with respect to safeguarding the privacy, security and transmission of individually identifiable health information that constitutes protected health information, including mandatory contractual terms and restrictions on the use and/or disclosure of such information without appropriate authorization;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal physician payment transparency requirements, sometimes referred to as the "Sunshine Act" under the Affordable Care Act, require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report to the Department of Health and Human Services information related to physician 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 laws and regulations in U.S. states, and in other countries, regions or localities in which we may do business, 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.

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, including activities that may be conducted by sales and marketing team we establish, 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 is 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.

Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business

Our Future Success Depends On Our Ability To Retain Key Executives And To Attract, Retain And Motivate Qualified Personnel.

We are highly dependent on the research and development, clinical, commercial and business development expertise of Dr. Samarth Kulkarni, our Chief Executive Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. 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 loss of the services of our executive officers or other key employees or consultants could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. For example, since our IPO our former Chief Executive Officer resigned in his role as Chief Executive Officer and became our President and Chairman of the Board of Directors, and our former Chief Financial Officer resigned. While we have promoted Samarth Kulkarni as our new Chief Executive Officer and hired Michael Tomsicek as our new Chief Financial Officer, there is no assurance that we will be able to find qualified replacements in a timely manner, if at all, in the event of the departure of other executive officers or key employees. If we are unable to retain high quality personnel, our ability to pursue our growth strategy will be limited.

We will also need to recruit and retain qualified scientific, clinical and commercial personnel as we advance the development of our product candidates and product pipeline. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific, clinical and commercial personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

In addition, being domiciled and organized in Switzerland may restrict our ability to attract, motivate and retain the required level of qualified personnel. In Switzerland, in 2013 legislation was adopted affecting compensation payable by public companies to members of its board of directors and executive team. Among other things, such legislation (i) imposes an annual binding shareholders' "say on pay" vote with respect to the compensation of executive management, including executive officers and the board of directors; (ii) prohibits severance, advances, transaction premiums and similar payments to executive officers and directors; and (iii) requires companies to specify various compensation-related matters in their articles of association, thus requiring them to be approved by a shareholders' vote.

We Will Need To Develop And Expand Our Company, And We May Encounter Difficulties In Managing This Development And Expansion, Which Could Disrupt Our Operations.

As of December 31, 2017, we had 127 full-time employees and we expect to increase our number of employees and the scope of our operations in 2018 and beyond as we conduct activities as a public company and seek to advance development and if successful, commercialization, of our product candidates. To manage our anticipated development and expansion, 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. Also, our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these expansion activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

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 in other jurisdictions, 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. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations, and prospects, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

If We Fail To Comply With Environmental, Health And Safety Laws And Regulations, We Could Become Subject To Fines Or Penalties Or Incur Costs That Could Harm Our Business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We contract with third parties for the disposal of these materials and wastes. We will not be able to eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from any use by us of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we anticipate obtaining product liability insurance coverage in advance of the commencement of any clinical trial of our product candidates, it may not be adequate to cover all liabilities that we may incur. Further, we anticipate that we will need to increase our insurance coverage if we successfully commercialize any product candidate. 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.

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

Product Liability Lawsuits Against Us Could Cause Us To Incur Substantial Liabilities And Could Limit Commercialization Of Any Product Candidates That We May Develop.

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

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

- the inability to commercialize any product candidates that we may develop.

Although we anticipate obtaining product liability insurance coverage in advance of the commencement of any clinical trial of our product candidates, it may not be adequate to cover all liabilities that we may incur. Further, we anticipate that we will need to increase our insurance coverage if we successfully commercialize any product candidate. 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 Fail To Establish And Maintain Proper And Effective Internal Control Over Financial Reporting, Our Operating Results And Our Ability To Operate Our Business Could Be Harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. 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 in accordance with generally accepted accounting principles. We have designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Our Internal Computer Systems, Or Those Of Our Collaborators Or Other Contractors Or Consultants, May Fail Or Suffer Security Breaches, Which Could Result In A Material Disruption Of Our Product Development Programs.

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

Our Business Is Subject To Economic, Political, Regulatory And Other Risks Associated With International Operations.

Our business is subject to risks associated with conducting business internationally. We and a number of our suppliers and collaborative and clinical study relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing regulatory requirements for drug approvals in non-U.S. countries;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;

- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling outside the United States;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities outside the United States;
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including floods and fires; and
- adverse effects and instability in global financial markets, political institutions and regulatory agencies resulting from the United Kingdom's June 23, 2016 vote to leave the European Union and subsequent invocation of Article 50 of the Lisbon Treaty on March 29, 2017.

Our Business Operations Have a Substantial International Footprint and We May Further Expand In The Future, Which Presents Challenges In Managing Our Business Operations.

We are headquartered in Zug, Switzerland and have offices in the U.S. and the United Kingdom. In addition, we may expand our international operations into other countries in the future. While we have acquired significant management and other personnel with substantial experience, conducting our business in multiple countries subjects us to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects, including, among other things:

- the increased complexity and costs inherent in managing international operations;
- diverse regulatory, financial and legal requirements, and any future changes to such requirements, in one or more countries where we are located or do business;
- country-specific tax, labor and employment laws and regulations;
- challenges inherent in efficiently managing employees in diverse geographies, including the need to adapt systems, policies, benefits and compliance programs to differing labor and other regulations;
- liabilities for activities of, or related to, our international operations or product candidates;
- changes in currency rates; and
- regulations relating to data security and the unauthorized use of, or access to, commercial and personal information.

As we continue to expand our operations, our corporate structure and tax structure has become substantially more complex. In connection with our current and future potential partnerships, we are actively engaged in developing and applying technologies and intellectual property with a view toward commercialization of products globally, often with commercialization partners. In connection with those activities, we already have and will likely continue to engage in complex cross-border and global transactions involving our technology, intellectual property and other assets, between CRISPR and other entities such as partners and licensees, and between companies within the CRISPR group. Such cross-border and global arrangements are both difficult to manage and can potentially give rise to complexities in areas such as tax treatment, particularly since we are subject to multiple tax regimes and different tax authorities can also take different views from each other, even as regards the same cross-border transaction or arrangement. There can be no assurance that we will effectively manage this increased complexity without experiencing operating inefficiencies, control deficiencies or tax liabilities. Significant management time and effort is required to effectively manage the increased complexity of our company, and our failure to successfully do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Risks Related to Intellectual Property

If We Are Unable To Adequately Protect Our Proprietary Technology Or Obtain And Maintain Patent Protection For The Products We Develop And For Our Technology And Product Candidates, 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 proprietary or intellectual property protection in the United States and other countries with respect to our CRISPR/Cas9 platform technology and any proprietary product candidates and technology we develop. Currently, no patents covering our CRISPR/Cas9 platform or product candidates have been issued to us in the United States and one of the patent applications we have licensed that may cover our platform was the subject of an interference proceeding at the United States Patent and Trademark Office, or USPTO; the termination of the interference proceeding has been appealed to the U.S. Court of Appeals for the Federal Circuit, or Federal Circuit, as discussed below. One patent covering our CRISPR/Cas9 platform was issued in Europe, but is the subject of opposition proceedings. We seek to protect our proprietary position by in-licensing intellectual property to cover our platform technology and filing patent applications in the United States and in other jurisdictions related to our technologies and product candidates that are important to our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position. If we or our licensors are unable to obtain or maintain patent protection with respect to our CRISPR/Cas9 platform technology and any proprietary products and technology we develop, our business, financial condition, results of operations and prospects could be materially harmed.

The scope of patent protection that will be available to us in the United States and in other countries is 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, or if any such patents will be found invalid, unenforceable or not infringed if challenged by our 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 know with any degree of certainty whether the inventors of our licensed patents and applications 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. Our owned and in-licensed patents may not cover such technology. If our competitors commercialize the CRISPR technology in conjunction with a protein other than Cas9, 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 in other jurisdictions. We may be subject to a third party preissuance submission of prior art to the USPTO, or a patent office in another jurisdiction, or become involved in opposition, derivation, revocation, reexamination, post-grant review and inter partes review, or interference proceedings, or litigation challenging our patent rights or the patent rights of others. Indeed, certain of our fundamental intellectual property has been subject to third party observations outside the United States and interference proceedings within the United States. Competitors may claim that they invented the inventions claimed in such issued patents or patent applications prior to our inventors, or may have filed patent applications before our inventors did. A competitor may also claim that our products and services infringe its patents and that we therefore cannot practice our technology as claimed under our patent applications, if issued. An adverse determination in any such claim may result in our inability to manufacture or commercialize products without infringing third-party patent rights. Competitors may also contest our patents, if issued, by showing that the invention was not patent-eligible, was not novel, was obvious or that the patent claims failed any other requirement for patentability. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights or allow third parties to commercialize our technology or products and compete directly with us, without payment to us. Moreover, we, or one of our licensors, may have to participate in additional interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a non-U.S. 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 freedom to operate, or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and 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. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

We Are Required To Pay Royalties Under Our License Agreements With Third-Party Licensors, And We Must Use Commercially Reasonable Diligence Efforts And Meet Milestones To Maintain Our License Rights.

Under our in-license agreements, including our in-license agreements with Dr. Emmanuelle Charpentier, we will be required to pay royalties based on our revenues from sales of our products utilizing the licensed technologies and these royalty payments could adversely affect the overall profitability for us of any products that we may seek to commercialize. Under each of our in-license agreements with, Dr. Charpentier, we have an obligation to use commercially reasonable efforts to develop and obtain regulatory approval to market a licensed therapeutic product. Our in-license agreements with Dr. Charpentier also include an obligation to file a U.S. Investigational New Drug application (or its equivalent in a major market country) by April 2021 and an obligation to file a U.S. Investigational New Drug application (or its equivalent in a major market country) by April 2024. We may not be successful in meeting these obligations in the future on a timely basis or at all. Our failure to meet these obligations may give Dr. Charpentier the right to terminate our license rights. We will need to outsource and rely on third parties for many aspects of the clinical development of the products covered under our license agreements. Delay or failure by these third parties could adversely affect our ability to meet our diligence obligations and the continuation of our license agreements with third-party licensors.

Some Of Our In-licensed Patent Applications Are Subject To Priority Disputes And Inventorship Disputes. Our Owned And In-Licensed Patents And Other Intellectual Property May Be Subject To Further Priority Disputes Or To Inventorship Disputes And Similar Proceedings. If We Or Our Licensors Are Unsuccessful In Any Of These Proceedings, We May Be Required To Obtain Licenses From Third Parties, Which May Not Be Available On Commercially Reasonable Terms Or At All, Or To Cease The Development, Manufacture, And Commercialization Of One Or More Of The Product Candidates We May Develop, Which Could Have A Material Adverse Impact On Our Business.

In January 2016, at our request, the USPTO declared an interference between one of the pending U.S. patent applications we licensed from Dr. Charpentier and twelve issued U.S. patents, and subsequently added one U.S. patent application, owned jointly by the Broad Institute and Massachusetts Institute of Technology and, in some instances, the President and Fellows of Harvard College, collectively referred to as the Broad. An interference is a proceeding conducted at the USPTO by the Patent Trial and Appeal Board, or PTAB, to determine which party was the first to invent subject matter claimed by both of these parties. There were two parties to this interference. Because our application was filed first, the USPTO designated Dr. Charpentier, the Regents of the University of California, or California, and the University of Vienna, or Vienna, collectively as "Senior Party" and designated Broad as "Junior Party." Following motions by the parties and other procedural matters, the PTAB concluded in February 2017 that the declared interference should be dismissed because the claim sets of the two parties were not directed to the same patentable invention in accordance with the PTAB's two-way test for patent interferences. In particular, the Junior Party's claims in the interference were all limited to uses in eukaryotic cells, while the Senior Party's claims in the interference were not limited to uses in eukaryotic cells but included uses in all settings. In April 2017, the Senior Party appealed the PTAB decision to the Federal Circuit, seeking review and reversal of the PTAB's February 2017 decision, which terminated the interference without determining which inventors actually invented the use of the CRISPR/Cas9 genome editing technology in eukaryotic cells. In parallel, either party can pursue existing or new patent applications in the U.S. and elsewhere. For example, one of the Broad's pending patent applications (U.S. Serial No. 14/523,799) issued as U.S. Patent No. 9,840,713 on December 12, 2017. Going forward, either party as well as other parties could seek a new interference related to the uses of the technology in eukaryotic cells or other aspects of the technology, and any existing or new patents could be the subject of other challenges to their validity of enforceability. In the context of a second interference or in other proceedings, a determination could be reached regarding that the Senior Party was not the first to invent, or it could be concluded that the contested subject matter is not patentable to the Senior Party and is patentable to the Junior Party, which in this case could preclude our U.S. patent applications from issuing as patents, in which case the proceedings would result in our losing the right to protect core innovations and our freedom to practice our core gene editing technology. If there is a second interference, either party can again appeal an adverse decision to the U.S. Court of Appeals for the Federal Circuit. In any case, it may be years before there is a final determination on priority. Pursuant to the terms of the license agreement with Dr. Charpentier, we are responsible for covering or reimbursing Dr. Charpentier's patent prosecution defense and related costs associated with our in-licensed technology.

Furthermore, we may be involved in other interference proceedings or other disputes in the future. For example, Toolgen Inc., or Toolgen, filed Suggestions of Interference in the USPTO on April 13, 2015, and December 3, 2015, suggesting that they believe some of the claims in pending U.S. applications owned by Toolgen (U.S. Serial No. 14/685,568 and U.S. Serial No. 14/685,510, respectively) interfere with certain claims in five of the Broad patents currently involved in the interference with Dr. Charpentier, California and Vienna. The USPTO may, in the future, declare an interference between our patent application and one or more Toolgen patent applications. We are also aware of additional third parties that have pending patent applications relating to CRISPR technologies, which similarly may or may not lead to further interference proceedings. For example, Rockefeller University has filed an application (U.S. Serial No. 15/217,489) claiming priority to an application filed by the Broad, but which names Rockefeller's employee Luciano Marraffini as co-inventor of CRISPR/Cas9 technology; Vilnius University has filed applications in the United States and in other jurisdictions (published internationally as WO2013/141680 and WO2013/142578 and granted as a patent in the United States as U.S. Patent No. 9,637,739), Harvard University has filed applications in the United States and in other jurisdictions (published internationally as WO2014/099744 and granted as a patent in the United States as U.S. Patent No. 9,023,649), and Sigma-Aldrich has filed applications in the United States and in other jurisdictions (published internationally as WO2014/089290), each claiming aspects of CRISPR/Cas9 technology based on applications claiming priority to provisional filings in 2012. Numerous other filings are based on provisional applications filed after 2012.

Broad, Toolgen, Vilnius, Harvard, Sigma-Aldrich and other parties routinely file international counterparts of their U.S. applications, some of which have been granted or could in future be granted in Europe and/or other non-U.S. jurisdictions. We and third parties have initiated opposition proceedings against some of these grants, and we may in the future oppose other grants to these or other applicants. For example, we and eight other entities have opposed European Patent 2771468 that was granted to Broad, MIT and Harvard. In hearings which began on January 16, 2018, the patent granted to Broad, MIT and Harvard was revoked, but the patentees are expected to appeal the decision against them. Oppositions are also now pending with respect to a number of other patents granted to them in Europe. Similarly, our intellectual property may in the future become involved in opposition proceedings in Europe or other jurisdictions. For example, the issued European patent we in-licensed from Dr. Charpentier has been opposed by multiple third parties. The opposition to the European patent could lead to the revocation of the patents in whole or in part, or could lead to the claims being narrowed in a way that could impair or preclude our ability to enforce the patent against competitors in Europe.

If we or our licensors are unsuccessful in any interference proceedings or other priority or validity disputes (including any patent oppositions) to which we or they are subject or become subject to, we may lose valuable intellectual property rights through the loss or narrowing of one or more of our patent applications. If we or our licensors are unsuccessful in any interference proceeding or other dispute, we may be required to seek to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other disputes. These third parties would be under no obligation to grant to us any such license and 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 and our partners may need to cease the practice of our core gene editing, and 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 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. If we are unsuccessful in our dispute with Broad, we and our partners may be blocked from commercializing any products based on our core gene editing technology. Even if we are successful in an interference proceeding or other similar disputes, it could result in substantial costs and be a distraction to management and other employees.

The Intellectual Property That Protects Our Core Gene Editing Technology Is Jointly Owned, And Our License Is From Only One Of The Joint Owners, Materially Limiting Our Rights In The United States And In Other Jurisdictions.

The family of patent applications we have in-licensed from Dr. Charpentier is the foundational patent protection for our core gene editing technology. However, that family includes other named inventors who assigned their rights either to California or to Vienna. As such, the intellectual property is currently co-owned by Dr. Charpentier, California, and Vienna. On December 15, 2016, we entered into a Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement, or IMA, with California, Vienna and their licensees including Caribou Biosciences, Inc. and Caribou's licensee Intellia Therapeutics, Inc. Under the IMA, the co-owners provided reciprocal worldwide cross-consents to each of the other co-owners' licensees and sublicensees, and agreed to a number of other commitments and obligations with respect to supporting and managing the underlying CRISPR/Cas9 gene editing intellectual property, including a cost-sharing agreement. As explained more fully below, that leaves us in a position of holding only non-exclusive or co-exclusive rights to the patent rights that protect our core gene editing technology, and we must continue to satisfy our contractual obligations under the IMA in order to maintain the effectiveness of the consents by California and Vienna to our license from Dr. Charpentier.

In the United States, each co-owner has the freedom to license and exploit the technology. As a result, we do not have exclusive access to any intellectual property rights that Dr. Charpentier co-owns with another entity, such as California and Vienna. Our license with Dr. Charpentier is therefore non-exclusive with respect to such co-owned rights. Furthermore, in the United States each co-owner is required to be joined as a party to any claim or action we may wish to bring to enforce those patent rights. Moreover, in the United States, non-exclusive licenses have no standing to bring a patent infringement action before a court. Therefore, for the patents owned with California and Vienna we have no ability to pursue third party infringement claims without cooperation of California and Vienna and potentially their licensees. Although we have entered into a Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement with Vienna and California and their licensees, which provides for, among other things, notice of and coordination in the event of third-party infringement of the CRISPR/Cas9 intellectual property, there can be no assurance that Vienna and California will cooperate with us in any future infringement. If we are unable to enforce our core patent rights licensed from Dr. Charpentier, we may be unable to prevent third parties from competing with us and may be unable to persuade companies to sublicense our technology, either of which could have a material adverse effect on our business.

If We Experience Disputes With The Third Parties That We In-license Intellectual Property Rights From, We Could Lose License Rights That Are Important To Our Business.

We license our foundational intellectual property from a third party, and we expect to continue to in-license additional third-party intellectual property rights as we expand our CRISPR/Cas9 gene-editing technology. Disputes may arise with the third parties from whom we license our intellectual property rights from for a variety of reasons, 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 and obligations associated with sublicensing;
- 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, or maintain consents under the IMA, are complex, and certain provisions in such agreements may be susceptible to multiple interpretations, or may conflict in such a way that puts us in breach of one or more agreements, which would make us susceptible to lengthy and expensive disputes with one or more of our licensing partners or the parties to the IMA. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

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 in-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 gene-editing technology and filing patent applications potentially relevant to our business. For example, we are aware of several third-party patent applications that, if issued, may be construed to cover our CRISPR/Cas9 technology and product candidates. In order to avoid infringing these third-party patents, we may find it necessary or prudent to obtain licenses from such third party intellectual property holders. We may also require licenses from third parties for certain modified or improved components of CRISPR/Cas9 technology, such as modified nucleic acids, as well as non-CRISPR/Cas9 technologies such as delivery methods that we are evaluating for use with product candidates we may develop. In addition, with respect to any patents we co-own with third parties, we may require licenses to such co-owners' interest to such patents. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for product candidates we may develop and CRISPR/Cas9 technology. The licensing or acquisition of third party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. 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, or discontinue the practice of our core CRISPR/Cas9 gene-editing technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Issued Patents Covering Our Technology And Product Candidates Could Be Found Invalid Or Unenforceable If Challenged In Court.

If we or one of our licensors initiated legal proceedings against a third party to enforce a patent covering a product candidate we may develop or our technology, including CRISPR/Cas9, 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 applications, such as our in-licensed CRISPR/Cas9 patent applications in the context of third party observations and oppositions filed in Europe and Australia, and may in the future raise similar claims before administrative bodies in the United States or in other jurisdictions, even outside the context of litigation. Mechanisms for challenging the validity of patents in patent offices include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in non-U.S. jurisdictions (e.g., opposition proceedings). Such proceedings could result in the loss of our patent applications or patents, or their narrowing 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. 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 Gene-Editing Technology, Including CRISPR/Cas9, Is Highly Dynamic, And Third Parties May Initiate And Prevail In Legal Proceedings Alleging That The Patents That We In-License Or Own Are Invalid Or 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 gene editing, especially in the area of CRISPR/Cas9 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, in addition to the ongoing interference 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 re-examination interference proceedings, post-grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in other jurisdictions such as oppositions before the European Patent Office. Third parties, including parties involved in ongoing interference proceedings, 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 including, for example, the Broad, Vilnius, Harvard and Sigma-Aldrich patents described above, that may be asserted to encompass our CRISPR/Cas9 technology. If we are unable to prove that these patents are invalid and we are not able to obtain or maintain a license on commercially reasonable terms, such third parties could potentially assert infringement claims against us, which could have a material adverse effect on the conduct of our business. If we are found to infringe such third-party patents, we and our partners may be required to pay damages, cease commercialization of the infringing technology, including our core CRISPR/Cas9 gene-editing technology, or obtain a license from such third parties, which may not be available on commercially reasonable terms or at all. Additionally, we have not performed any freedom-to-operate analysis on specific product candidates at this stage to identify potential infringement risks. A proper analysis of that type will not be feasible until specific product candidates are designed.

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, ownership, 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.

Intellectual Property Litigation Could Cause Us To Spend Substantial Resources And Distract Our Personnel From Their Normal Responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities and generally harm our business. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation in certain countries, including the United States, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments 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 shares. 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 adequately conduct such litigation or proceedings. 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. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing or misappropriating or successfully challenging our intellectual property rights. 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.

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. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and other patent agencies over the lifetime of the patent. 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. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, we may not be able to stop a competitor from marketing drugs that are the same as or similar to our product candidates, which would have a material adverse effect on our business.

Some Intellectual Property Which We Have In-licensed May Have Been Discovered Through Government Funded Programs And Thus May Be Subject To Federal Regulations Such As "march-in" Rights, Certain Reporting Requirements And A Preference For U.S.-based Manufacturers. Compliance With Such Regulations May Limit Our Exclusive Rights, And Limit Our Ability To Contract With Non-U.S. Manufacturers.

The intellectual property rights to which we have in-licensed under Dr. Charpentier's joint interest are co-owned by California, which has indicated that the invention was made under Grant No. GM081879 awarded by the National Institute of Health. These rights are therefore subject to certain federal regulations. The U.S. government has certain rights pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act, to patents covering government rights in certain inventions developed under a government-funded program. These rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations, also referred to as "march-in rights." The U.S. government also has the right to take title to these inventions if we, or the applicable contractor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable contractor to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future patents covering inventions is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

We May Not Be Able To Protect Our Intellectual Property And Proprietary Rights Throughout The World.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in intellectual property laws various jurisdictions worldwide. Additionally, the patent laws of some countries do not afford intellectual property protection to the same extent as the laws of the United States. For example, unlike patent law in the United States, the patent law in Europe and many other jurisdictions precludes the patentability of methods of treatment of the human body and imposes substantial restrictions on the scope of claims it will grant if broader than specifically disclosed embodiments.

Many companies have encountered significant problems in protecting and defending intellectual property rights in various jurisdictions globally. 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 pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. 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 various jurisdictions globally 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 third parties, including 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. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Changes To The Patent Law In The United States And Other Jurisdictions Could Diminish The Value Of Patents In General, Thereby Impairing Our Ability To Protect Our Product Candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a “first to file” system. The first-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and 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 harm our business, results of operations and financial condition.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. For example, in *Association for Molecular Pathology v. Myriad Genetics, Inc*., the Supreme Court ruled that a “naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated,” and invalidated Myriad Genetics’ claims on the isolated BRCA1 and BRCA2 genes. Certain claims of our patents relate to CRISPR/Cas9 gene-editing technology as well as guide components that are directed to naturally occurring DNA sequences. To the extent that such claims are deemed to be directed to natural products, or to lack an inventive concept above and beyond an isolated natural product, a court may decide the claims are invalid under *Myriad*. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Europe’s planned Unified Patent Court may particularly present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. While that new court is being implemented to provide more certainty and efficiency to patent enforcement throughout Europe, it will also provide our competitors with a new forum to use to centrally revoke our European patents. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by that court. We will have the right to opt our patents out of that system over the first seven years of the court, but doing so may preclude us from realizing the benefits of the new unified court.

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. 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, or those to whom they communicate it, 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, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or if the term of any such extension is less than we request, we will be unable to rely on our patent position to forestall the marketing 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.

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. 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.

Risks Related to The Ownership of Our Common Shares

We Will Incur Increased Costs As A Result Of Operating As A Public Company And Our Management Will Be Required To Devote Substantial Time To New Compliance Initiatives And Corporate Governance Practices.

As a public company, and particularly after we are no longer an "emerging growth company," we will incur significant legal, accounting and other expenses that we did not incur as a private company. SOX, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Market, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. Moreover, these requirements will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, the rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We are currently evaluating these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. 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, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not 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 financial statements.

The Market Price Of Our Common Shares Has Been Volatile and Fluctuate Substantially, Which Could Result In Substantial Losses For Shareholders.

Our share price has been and in the future, may be subject to substantial volatility. In addition, the stock market in general, and Nasdaq listed and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. For example, our shares traded within a range of a high price of $25.00 and a low price of $11.63 per share for the period beginning on October 19, 2016, our first day of trading on the Nasdaq Global Market, through December 29, 2017. As a result of this volatility, our shareholders could incur substantial losses. In addition, the market price for our common shares may be influenced by many factors, including:

- the success of existing or new competitive products or technologies;
- the timing and results of any product candidates that we may develop;
- commencement or termination of collaborations for our product development and research programs;
- failure or discontinuation of any of our product development and research programs;
- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- developments or changing views regarding the use of genomic products, including those that involve gene editing;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs, or product candidates that we may develop;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common shares by us, our insiders, or other shareholders;
- expiration of market stand-off or lock-up agreements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our common shares;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

These and other market and industry factors may cause the market price and demand for our common shares to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their common shares and may otherwise negatively affect the liquidity of our common shares. In the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our shareholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

If Securities Analysts Do Not Publish Research Or Reports About Our Business Or If They Publish Negative Evaluations Of Our Common Shares, The Price Of Our Common Shares Could Decline.

The trading market for our common shares will rely 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 common shares, the price of our common shares could decline. If one or more of these analysts cease to cover our common shares, we could lose visibility in the market for our common shares, which in turn could cause our common share price to decline.

A Significant Portion Of Our Total Outstanding Common Shares May Be Sold Into The Market In The Near Future, Which Could Cause The Market Price Of Our Common Shares To Decline Significantly, Even If Our Business Is Doing Well.

Sales of a substantial number of our common shares 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 common shares intend to sell shares, could reduce the market price of our common stock.

All lock-up agreements entered into in connection with our initial public offering are expected to expire on April 17, 2017. Following the lockup expiration, outstanding common shares may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act of 1933, as amended (the "Securities Act"), or to the extent that such shares have already been registered under the Securities Act and are held by non-affiliates of ours.

Moreover, holders of a substantial number of our common shares have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also have registered substantially all common shares that we may issue under our equity compensation plans or that are issuable upon exercise of outstanding options. These common shares can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates. If any of these additional common shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common shares could decline.

Our Executive Officers, Directors, And Principal Stockholders, If They Choose To Act Together, Have The Ability To Control All Matters Submitted To Stockholders For Approval.

As of February 28, 2018, common shares beneficially owned by our executive officers, directors and principal shareholders, including Vertex, Bayer Healthcare and other shareholders and their affiliates who owned more than 5% of our outstanding common shares totaled 26,538,395. As a result, these shareholders, if they were to act together, would be able to influence our management and affairs and all matters requiring shareholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common shares.

*We Have Broad Discretion In The Use Of Our Cash Reserves And May Not Use Such Cash Reserves 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 shares. 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 shares 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 Are An "Emerging Growth Company," And The Reduced Disclosure Requirements Applicable To Emerging Growth Companies May Make Our Common Shares Less Attractive To Investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more; (ii) December 31, 2021, being the last day of the fiscal year following the fifth anniversary of the date of the completion of the IPO; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, which means the market value of our common shares that is held by non-affiliates exceeds $700 million as of the prior June 30th. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of SOX;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- being permitted to present only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this Annual Report on Form 10-K;
- reduced disclosure obligations regarding executive compensation; and
- the "say on pay" provisions (requiring a non-binding shareholder vote to approve compensation of certain executive officers) the "say on golden parachute" provisions (requiring a non-binding shareholder vote to approve golden parachute arrangements for certain executive officers in connection with mergers and certain other business combinations) of the Dodd-Frank Wall Street Reform and Protection Act, or Dodd-Frank Act, and some of the disclosure requirements of the Dodd-Frank Act relating to compensation of our chief executive officer.

We may choose to take advantage of some, but not all, of the available exemptions. We cannot predict whether investors will find our common shares less attractive if we rely on these exemptions. If some investors find our common shares less attractive as a result, there may be a less active trading market for our common shares and our common share price may be more volatile.

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

We Do Not Expect To Pay Dividends In The Foreseeable Future.

We have not paid any dividends since our incorporation. Even if future operations lead to significant levels of distributable profits, we currently intend that any earnings will be reinvested in our business and that no dividends will be paid prior to the time we have an established revenue stream to support continuing dividends. The proposal to pay future dividends to shareholders will in addition effectively be at the discretion of our board of directors and shareholders after taking into account various factors including our business prospects, cash requirements, financial performance and new product development. In addition, payment of future dividends is subject to certain limitations pursuant to Swiss law or by our articles of association. Accordingly, investors cannot rely on dividend income from our common shares and any returns on an investment in our common shares will likely depend entirely upon any future appreciation in the price of our common shares. Dividends, if any, paid on our common shares are subject to Swiss federal withholding tax, except if paid out of reserves from capital contributions ("*Kapitaleinlagen*").

We Are A Swiss Corporation. The Rights Of Our Shareholders May Be Different From The Rights Of Shareholders In Companies Governed By The Laws Of U.S. Jurisdictions.

We are a Swiss corporation. Our corporate affairs are governed by our articles of association and by Swiss law. The rights of our shareholders and the responsibilities of members of our board of directors may be different from the rights and obligations of shareholders and directors of companies governed by the laws of U.S. jurisdictions. In the performance of its duties, our board of directors is required by Swiss law to consider the interests of our Company, our shareholders and our employees with due observation of the principles of reasonableness and fairness. It is possible that the board of directors will consider interests that are different from, or in addition to, your interests as a shareholder. Swiss corporate law limits the ability of our shareholders to challenge resolutions made or other actions taken by our board of directors in court. Our shareholders generally are not permitted to file a suit to reverse a decision or an action taken by our board of directors but are instead only permitted to seek damages for breaches of the duty of care and loyalty. As a matter of Swiss law, shareholder claims against a member of our board of directors for breach of the duty of care and loyalty would have to be brought in Zug, Switzerland, or where the relevant member of our board of directors is domiciled. In addition, under Swiss law, any claims by our shareholders against us must be brought exclusively in Zug, Switzerland.

Our Common Shares Are Issued Under The Laws Of Switzerland, Which May Not Protect Investors In A Similar Fashion Afforded By Incorporation In A U.S. State.

We are organized under the laws of Switzerland. However, there can be no assurance that Swiss law will not change in the future or that it will serve to protect investors in a similar fashion afforded under corporate law principles in the U.S., which could adversely affect the rights of investors.

Our Status As A Swiss Corporation Means That Our Shareholders Enjoy Certain Rights That May Limit Our Flexibility To Raise Capital, Issue Dividends And Otherwise Manage Ongoing Capital Needs And May Cause Us To Be Unable To Make Distributions Without Subjecting Our Shareholders To Swiss Withholding Tax.

Swiss law allows our shareholders to authorize share capital that can be issued by the board of directors without additional shareholder approval. This authorization is limited to 50% of the existing registered share capital and must be renewed by the shareholders every two years. Additionally, subject to specified exceptions, Swiss law grants preemptive rights to existing shareholders to subscribe to any new issuance of shares. Swiss law also does not provide as much flexibility in the various terms that can attach to different classes of shares as the laws of some other jurisdictions. Swiss law also reserves for approval by shareholders certain corporate actions over which a board of directors would have authority in some other jurisdictions. For example, the payment of dividends and the cancellation of treasury shares must be approved by shareholders. These Swiss law requirements relating to our capital management may limit our flexibility, and situations may arise where greater flexibility would have provided substantial benefits to our shareholders.

Under Swiss law, a Swiss corporation may pay dividends only if the corporation has sufficient distributable profits from previous fiscal years, or if the corporation has distributable reserves, each as evidenced by its audited statutory balance sheet, and after allocations to reserves required by Swiss law and our articles of association have been deducted. Freely distributable reserves are generally booked either as “free reserves” or as “capital contributions” (*Kapitaleinlagen*, contributions received from shareholders) in the “reserve from capital contributions.” Distributions may be made out of registered share capital—the aggregate par value of a company’s registered shares—only by way of a capital reduction. We will not be able to pay dividends or make other distributions to shareholders on a Swiss withholding tax-free basis in excess of our aggregate qualifying contributions and registered share capital unless we increase our share capital or our reserves from capital contributions. We would also be able to pay dividends out of distributable profits or freely distributable reserves, but such dividends would be subject to Swiss withholding taxes. There can be no assurance that we will have sufficient distributable profits, free reserves, reserves from capital contributions or registered share capital to pay a dividend or effect a capital reduction, that our shareholders will approve dividends or capital reductions proposed by us or that we will be able to meet the other legal requirements for dividend payments or distributions as a result of capital reductions.

Generally, Swiss withholding tax of 35% is due on dividends and similar distributions to our shareholders, regardless of the place of residency of the shareholder, unless the distribution is made to shareholders out of (i) a reduction of registered share capital or (ii) assuming certain conditions are met, qualifying capital contribution reserves, as further described under "Taxation—Swiss Tax Considerations—Swiss Federal Withholding Tax". A U.S. holder that qualifies for benefits under the Convention between the United States of America and Switzerland for the Avoidance of Double Taxation with Respect to Taxes on Income, or the U.S.-Swiss Treaty, may apply for a refund of the tax withheld in excess of the 15% treaty rate (or in excess of the 5% reduced treaty rate for qualifying corporate shareholders with at least 10% participation in our voting shares, or for a full refund in the case of qualified pension funds). There can be no assurance that we will have sufficient qualifying capital contribution reserves to pay dividends free from Swiss withholding tax, or that Swiss withholding rules will not be changed in the future. In addition, we cannot provide assurance that the current Swiss law with respect to distributions out of qualifying capital contribution reserves will not be changed or that a change in Swiss law will not adversely affect us or our shareholders, in particular as a result of distributions out of qualifying capital contribution reserves becoming subject to additional corporate law or other restrictions. There are currently ongoing discussions in the Swiss Parliament that may limit the distribution of qualifying capital contributions. In addition, over the long term, the amount of registered share capital available to us for registered share capital reductions or qualifying capital contributions available to us to pay out as distributions is limited. If we are unable to make a distribution through a reduction in par value or out of qualifying capital contributions, we may not be able to make distributions without subjecting our shareholders to Swiss withholding taxes.

Under present Swiss tax laws, repurchases of shares for the purposes of cancellation are treated as a partial liquidation subject to 35% Swiss withholding tax on the difference between the repurchase price and the par value except, since January 1, 2011, to the extent attributable to qualifying capital contributions (*Kapitaleinlagen*) if any, the Swiss withholding becomes due. No partial liquidation treatment applies and no withholding tax is triggered if the shares are not repurchased for cancellation but held by us as treasury shares. However, should we not resell such treasury shares within six years, the withholding tax becomes due at the end of the six-year period.

Certain U.S. Shareholders May Be Subject To Adverse U.S. Federal Income Tax Consequences If We Are A Controlled Foreign Corporation.

Each "Ten Percent Shareholder" (as defined below) in a non-U.S. corporation that is classified as a "controlled foreign corporation," or a CFC, for United States federal income tax purposes generally is required to include in income for U.S. federal tax purposes such Ten Percent Shareholder's pro rata share of the CFC's "Subpart F income" and investment of earnings in U.S. property, even if the CFC has made no distributions to its shareholders. Subpart F income generally includes dividends, interest, rents and royalties, gains from the sale of securities and income from certain transactions with related parties. In addition, a Ten Percent Shareholder that realizes gain from the sale or exchange of shares in a CFC may be required to classify a portion of such gain as dividend income rather than capital gain. A non-U.S. corporation generally will be classified as a CFC for United States federal income tax purposes if Ten Percent Shareholders own, directly or indirectly, more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A "Ten Percent Shareholder" is a United States person (as defined by the U.S. Internal Revenue Code of 1986, as amended (the "Code")) who owns or is considered to own 10% or more of the total combined voting power of all classes of stock entitled to vote of such corporation. The determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain.

During our 2017 taxable year we believe that we had certain shareholders that were Ten Percent Shareholders for United States federal income tax purposes. However, our CFC status for the taxable year ended December 31, 2017 and our current taxable year is unknown and we may be a CFC for the taxable year ended December 31, 2017, our current taxable year or a following year. In addition, recent changes to the attribution rules relation to the determination of CFC status may make it difficult to determine our CFC status for any taxable year. U.S. holders should consult their own tax advisors with respect to the potential adverse U.S. tax consequences of becoming a Ten Percent Shareholder in a CFC. If we are classified as both a CFC and a PFIC, we generally will not be treated as a PFIC with respect to those U.S. holders that meet the definition of a Ten Percent Shareholder during the period in which we are a CFC.

Certain U.S. Shareholders May Be Subject to Adverse Tax Consequences If We Are A Passive Foreign Investment Company.

Generally, if, for any taxable year, at least 75% of our gross income is passive income, or at least 50% of the value of our assets is attributable to assets that produce passive income or are held for the production of passive income, including cash, we would be characterized as a PFIC, for U.S. federal income tax purposes. For purposes of these tests, passive income includes dividends, interest, and gains from the sale or exchange of investment property and rents and royalties other than rents and royalties which are received from unrelated parties in connection with the active conduct of a trade or business. If we are characterized as a PFIC, U.S. holders of our common shares may suffer adverse tax consequences, including having gains realized on the sale of the common shares treated as ordinary income, rather than capital gain, the loss of the preferential rate applicable to dividends received on the common shares by individuals who are U.S. holders, and having interest charges apply to distributions by us and the proceeds of sales of the common shares.

Our status as a PFIC will depend on the composition of our income and the composition and value of our assets which may be determined in part by reference to the quarterly market value of our common shares, which may be volatile. Our status may also depend, in part, on how, and how quickly, we utilize the cash proceeds from the IPO in our business. Our status as a PFIC is a fact-intensive determination made on an annual basis and we cannot provide any assurances regarding our PFIC status for any past, current or future taxable years.

Because it is possible we were a PFIC for the 2016 taxable year, we provided the information that is necessary for you to make a QEF election with respect to us for the 2016 taxable year on our website (www.crisprtx.com). In addition, although we have not yet determined whether we are a PFIC for the 2017 taxable year, it is possible that we may be a PFIC for the 2017 taxable year as well. We will endeavor to provide you, for each taxable year that we determine we are a PFIC, a PFIC Annual Information Statement containing information necessary for you to make a QEF election with respect to us.

If we are determined to be a PFIC, a U.S. holder will generally be treated as owning a proportionate amount (by value) of shares owned by us in any of our direct or indirect subsidiaries that are also PFICs, each a lower-tier PFIC, and will be subject to similar adverse rules with respect to distributions from, or dispositions of, such lower-tier PFICs, in each case as if such U.S. holder held such shares directly (even if such U.S. holder does not receive the proceeds of such distributions or dispositions directly). We have not determined whether any of our subsidiaries (including TRACR Hematology Ltd. and CRISPR Therapeutics Ltd.) are or may be lower-tier PFICs for any prior taxable year, the current taxable year or future taxable years, and we do not intend to do so. We also do not intend to make available the information necessary for U.S. holders to make a QEF election with respect to any lower-tier PFICs and therefore you should expect that you will not be able to make a QEF election with respect to them.

You are urged to consult your own tax advisors regarding our PFIC status and the tax considerations relevant to an investment in a PFIC, including the availability, and advisability, of, and procedure for making, a QEF election with respect to us, and the application of the PFIC rules to any of our subsidiaries.

Comprehensive Tax Reform Legislation Could Adversely Affect Our Business And Financial Condition.

On December 22, 2017, the “Tax Cuts and Jobs Act” (TCJA) was enacted. The TCJA significantly reforms the Internal Revenue Code of 1986, as amended (the “Code”). The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and puts into effect the migration from a “worldwide” system of taxation to a territorial system. We continue to examine the impact this tax reform legislation may have on our business. The impact of this tax reform is uncertain and could be adverse.

U.S. Shareholders May Not Be Able To Obtain Judgments Or Enforce Civil Liabilities Against Us Or Our Executive Officers Or Members Of Our Board Of Directors.

We are a Swiss corporation organized under the laws of Switzerland and our registered office and domicile is located in Basel, Switzerland. Moreover, certain of our directors and executive officers and a number of directors of each of our subsidiaries are not residents of the United States, and all or a substantial portion of the assets of such persons are located outside the United States. As a result, it may not be possible for investors to effect service of process within the United States such persons or to enforce against them judgments obtained in U.S. courts, including judgments in actions predicated upon the civil liability provisions of the federal securities laws of the United States. We have been advised by our Swiss counsel that there is doubt as to the enforceability in Switzerland of original actions, or in actions for enforcement of judgments of U.S. courts, of civil liabilities to the extent solely predicated upon the federal and state securities laws of the United States. Original actions against persons in Switzerland based solely upon the U.S. federal or state securities laws are governed, among other things, by the principles set forth in the Swiss Federal Act on Private International Law. This statute provides that the application of provisions of non-Swiss law by the courts in Switzerland shall be precluded if the result is incompatible with Swiss public policy. Also, mandatory provisions of Swiss law may be applicable regardless of any other law that would otherwise apply.

Switzerland and the United States do not have a treaty providing for reciprocal recognition and enforcement of judgments in civil and commercial matters. The recognition and enforcement of a judgment of the courts of the United States in Switzerland is governed by the principles set forth in the Swiss Federal Act on Private International Law. This statute provides in principle that a judgment rendered by a non-Swiss court may be enforced in Switzerland only if:

- the non-Swiss court had jurisdiction pursuant to the Swiss Federal Act on Private International Law;
- the judgment of such non-Swiss court has become final and non-appealable;
- the judgment does not contravene Swiss public policy;

- the court procedures and the service of documents leading to the judgment were in accordance with the due process of law; and
- no proceeding involving the same position and the same subject matter was first brought in Switzerland, or adjudicated in Switzerland, or was earlier adjudicated in a third state and this decision is recognizable in Switzerland.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our principal executive offices are located in Zug, Switzerland pursuant to a real estate lease agreement with a term that renews every six months. We also have facilities in Cambridge, Massachusetts, where we occupy approximately 65,376 square feet of laboratory and office space under a sublease that expires in December 2026. We also lease approximately 19,817 square feet of additional office and laboratory space in Cambridge, Massachusetts pursuant to a lease that expires in February 2022. In London, England, we occupy and maintain office space pursuant to a real estate lease agreement with a term that renews every six months. We believe that our facilities are adequate for our current needs and that suitable additional or substitute space would be available if 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 are currently no claims or actions pending against us that, in the opinion of our management, are likely to have a material adverse effect on our business. In January 2016, the United States Patent and Trademark Office, or USPTO, declared an interference between one of the pending U.S. patent applications we have in-licensed from Dr. Charpentier and twelve issued U.S. patents and one U.S. patent application owned jointly by The Broad Institute, Massachusetts Institute of Technology, President and Fellows of Harvard College, or Broad. The interference was redeclared in March 2016 to add a U.S. patent application owned by Broad. An interference is a proceeding conducted at the USPTO by the Patent Trial and Appeal Board, or PTAB, to determine which party was first to invent subject matter by at least two parties. There are currently two parties to this interference. Our in-licensed patent application is co-owned among Dr. Charpentier, the Regents of the University of California, and the University of Vienna, whom the USPTO designated collectively as "Senior Party"; Broad was designated as "Junior Party." Following motions by the parties and other procedural matters, the PTAB concluded in February 2017 that the declared interference should be dismissed because the claim sets of the two parties were not directed to the same patentable invention in accordance with the PTAB's two-way test for patent interferences. In particular, the Junior Party's claims in the interference were all limited to uses in eukaryotic cells, while the Senior Party's claims in the interference were not limited to uses in eukaryotic cells but included uses in all settings. Senior Party appealed the decision to the U.S. Court of Appeals for the Federal Circuit. In parallel, either party can also pursue existing or new patent applications in the U.S. and elsewhere. Going forward, either party as well as other parties could seek a new interference related to the uses of the technology in eukaryotic cells or other aspects of the technology, and any existing or new patents could be the subject of other challenges to their validity of enforceability. In the context of a second interference or in other proceedings, a determination could be reached regarding that the Senior Party was not the first to invent, or it could be concluded that the contested subject matter is not patentable to the Senior Party and is patentable to the Junior Party, which in this case could preclude our U.S. patent applications from issuing as patents, in which case the proceedings would result in our losing the right to protect core innovations and our freedom to practice our core gene editing technology. If there is a second interference, either party could again appeal an adverse decision to the U.S. Court of Appeals for the Federal Circuit. In any case, it may be years before there is a final determination on priority. In addition, both the Broad Toolgen Inc. and Sigma have filed international counterparts of their U.S. applications, some of which were granted in Europe and/or other jurisdictions, and Vilnius University and other third parties also have international counterparts of U.S. patent applications that could proceed to grant. We and third parties have initiated opposition proceedings against some of these grants, and we may in the future oppose other grants to these or other applicants. Similarly, if we should obtain patent grants in the U.S., Europe and other jurisdictions, these could also be the subject of oppositions or other post-grant procedures sought by third parties in order to revoke the grants or narrow the scope of granted claims. Going forward, with existing and new challenges being filed against CRISPR/Cas9 cases in the U.S., Europe and elsewhere, and considering the number of interested parties, it is reasonable to expect that patents directed to the underlying technology will continue to be the subject of ongoing disputes over at least the next several years, and potentially beyond as decisions in favor or against particular parties may be the subject of appeals.

For further information regarding risks regarding the interference and patent rights held by third parties, please see "Risk Factors—Risks Related to Our Intellectual Property" contained in Item 1A of this report.

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 is traded on The Nasdaq Global Market under the symbol “CRSP.” The following table sets forth for the periods indicated the high and low sale prices per share of our common stock as reported by Nasdaq Stock Market LLC:

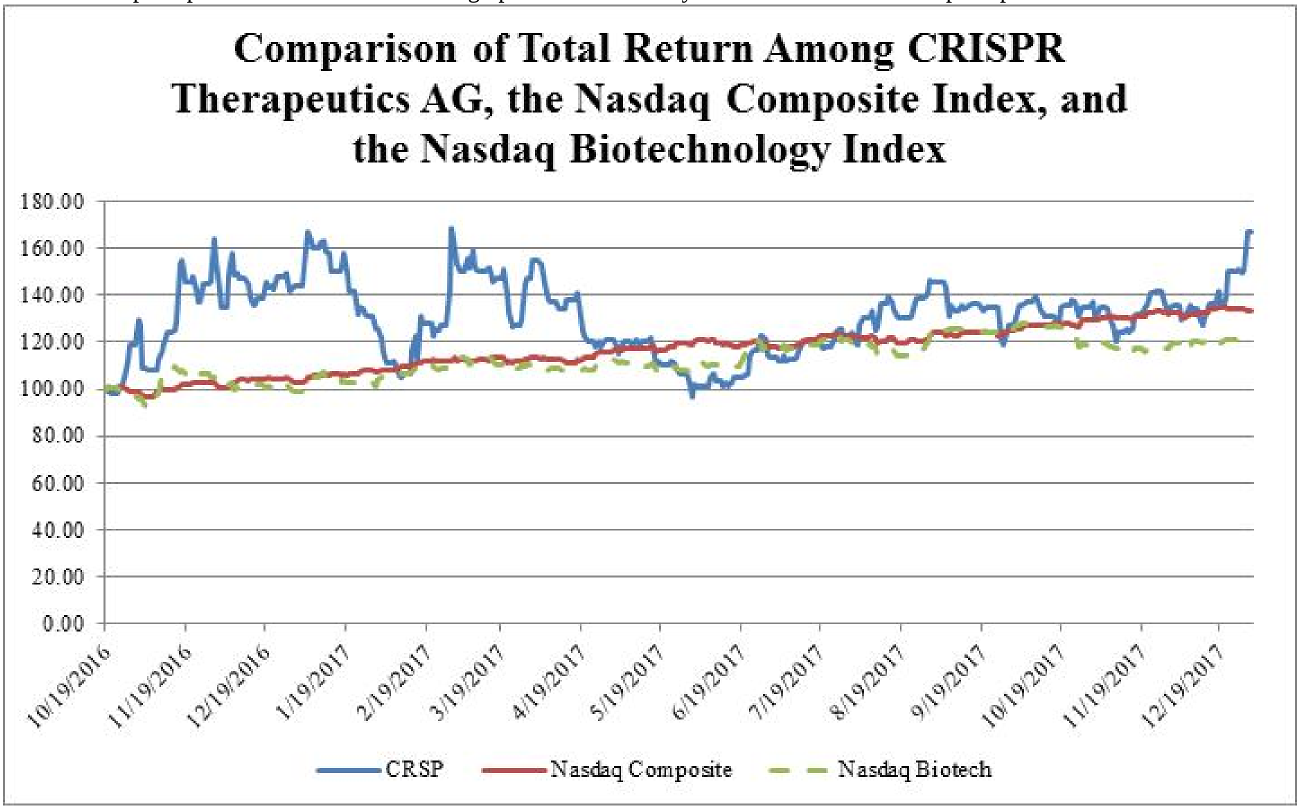
Year Ended December 31, 2017:	High	Low
First quarter	$ 24.99	$ 11.63
Second quarter	22.22	13.50
Third quarter	21.32	15.55
Fourth quarter	25.00	16.51

Year Ended December 31, 2016:	High	Low
Fourth quarter	$ 23.97	$ 13.75

Stock Performance Graph

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

The graph set forth below compares the cumulative total stockholder return on our shares between October 19, 2016 (the date of our initial public offering) and December 29, 2017, with the cumulative total return of (a) the Nasdaq Biotechnology Index and (b) the Nasdaq Composite Index, over the same period. This graph assumes the investment of $100 on October 19, 2016 in our common stock, the Nasdaq Biotechnology Index and the Nasdaq Composite Index and assumes the reinvestment of dividends, if any. The graph assumes our closing sales price on October 19, 2016 of $14.09 per share as the initial value of our common shares and not the initial offering price to the public of $14.00 per share. The comparisons shown in the graph below are based upon historical data. The stock price performance included in this graph is not necessarily indicative of future stock price performance.



Holders

As of February 28, 2018, we had approximately 19 holders of record of our common shares. This number does not include beneficial owners whose shares were held in street name.

Dividends

We have not paid any cash dividends on our common shares since inception and do not anticipate paying cash dividends in the foreseeable future.

Securities authorized for issuance under equity compensation plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Purchase of Equity Securities

There were no repurchases of our common shares made during the year ended December 31, 2017.

Item 6. Selected Financial Data.

SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated financial data should be read in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations”, the consolidated financial statements and related notes, and other financial information included in this Annual Report on Form 10-K.

The consolidated statements of operations data for the years ended December 31, 2017, 2016, 2015 and 2014 and the consolidated balance sheet data as of December 31, 2017, 2016 and 2015 are derived from our audited consolidated financial statements included in this Annual Report on Form 10-K. Historical results are not necessarily indicative of the results to be expected in future periods.

	December 31, 2017	2016	2015	2014
	(in thousands, except share and per share amounts)			
Consolidated Statements of Operations Data:				
Collaboration revenue	$ 40,997	$ 5,164	$ 247	$ —
Operating expenses:				
Research and development	69,800	42,238	12,573	1,513
General and administrative	35,845	31,056	13,403	5,114
Total operating expenses	105,645	73,294	25,976	6,627
Loss from operations	(64,648)	(68,130)	(25,729)	(6,627)
Other (expense) income, net	(1,960)	45,412	(92)	(236)
Net loss before (provision for) benefit from income taxes	(66,608)	(22,718)	(25,821)	(6,863)
(Provision for) benefit from income taxes	(1,749)	(484)	(7)	63
Net loss	(68,357)	(23,202)	(25,828)	(6,800)
Foreign currency translation adjustment	40	(18)	(6)	(2)
Comprehensive loss	$ (68,317)	(23,220)	$ (25,834)	$ (6,802)
Reconciliation of net loss to net loss attributable to common shareholders:				
Net loss	$ (68,357)	$ (23,220)	$ (25,828)	$ (6,800)
Loss attributable to noncontrolling interest	—	25	325	536
Loss on extinguishment of redeemable convertible preferred shares	—	—	—	(745)
Net loss attributable to common shareholders	$ (68,357)	$ (23,177)	$ (25,503)	$ (7,009)
Net loss per share attributable to common shareholders, basic and diluted	$ (1.71)	$ (1.89)	$ (5.06)	$ (1.97)
Weighted-average common shares outstanding, basic and diluted	40,057,365	12,257,483	5,037,404	3,559,985

	December 31, 2017	2016	2015
	(in thousands)		
Consolidated Balance Sheet Data:			
Cash	$ 239,758	$ 315,520	$ 155,961
Working capital	233,874	298,190	146,685
Total assets	271,346	344,962	159,423
Redeemable convertible preferred shares	—	—	64,521
Total shareholders’ equity	187,832	232,846	(29,124)

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

You should read the following discussion and analysis of our financial condition and results of operations together with the section entitled “Selected Consolidated Financial Data” and 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, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a leading gene editing company focused on the development of CRISPR/Cas9-based therapeutics. CRISPR/Cas9 is a revolutionary gene editing technology that allows for precise, directed changes to genomic DNA. The application of CRISPR/Cas9 for gene editing was co-invented by one of our scientific founders, Dr. Emmanuelle Charpentier, who, along with her collaborators, published work elucidating how CRISPR/Cas9, a naturally occurring viral defense mechanism found in bacteria, can be adapted for use in gene editing. We are applying this technology to potentially treat a broad set of rare and common diseases by disrupting, correcting or regulating the genes related to the disease. We believe that our scientific expertise, together with our approach, may enable an entirely new class of highly active and potentially curative treatments for patients for whom current biopharmaceutical approaches have had limited success.

Since our inception in October 2013, we have devoted substantially all of our resources to our research and development efforts, identifying potential product candidates, undertaking drug discovery and preclinical development activities, building and protecting our intellectual property portfolio, organizing and staffing our company, business planning, raising capital, and providing general and administrative support for these operations. To date, we have primarily financed our operations through private placements of our preferred shares, common stock issuances, convertible loans and collaboration agreements with strategic partners.

In January 2018, we completed an offering of 5,750,000 of our common shares, which were sold at a price of $22.75 per share. This offering resulted in $122.6 million of net proceeds to the Company. The underwriting discount of $7.8 million and other expenses of $0.4 million related to the equity offering were recorded as an offset to additional paid-in capital.

All of our revenue to date has been collaboration revenue. We have incurred significant net operating losses in every year since our inception and expect to continue to incur net operating losses for the foreseeable future. As of December 31, 2017, we had $239.8 million in cash and an accumulated deficit of $125.4 million. We expect to continue to incur significant expenses and increasing operating losses for the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase significantly as we continue our current research programs and development activities; seek to identify additional research programs and additional product candidates, conduct initial drug application supporting preclinical studies and initiate clinical trials for our product candidates; initiate preclinical testing and clinical trials for any other product candidates we identify and develop, maintain, expand and protect our intellectual property portfolio, further develop our gene editing platform; hire additional research, clinical and scientific personnel; and incur additional costs associated with operating as a public company.

Collaboration Agreement, Joint Development and Commercialization Agreement- Vertex

In October 2015, we entered into a strategic research collaboration agreement with Vertex focused on the development of CRISPR/Cas9-based therapies. Under the terms of our agreement, we received an upfront, nonrefundable payment of $75.0 million and $30.0 million in convertible loan proceeds.

In December 2017, we and Vertex entered into Amendment No. 1 to the Collaboration Agreement, or the (the “Amendment”). The Amendment, among other things, modified certain definitions and provisions of the Collaboration Agreement to make them consistent with the JDA and clarified how many options are exercised (or deemed exercised) in connection with certain targets specified under the Collaboration Agreement. The Amendment also amended other provisions of the Collaboration Agreement, including the expiration terms of the Collaboration Agreement.

In December 2017, we entered into a Joint Development and Commercialization Agreement, or JDA, with Vertex for the development and commercialization of CTX001. The initial focus of the JDA centers on developing CTX001 for beta-thalassemia and SCD. In connection with entering into the JDA, we received a $7.0 million up-front payment from Vertex and are eligible for a one-time low seven-digit milestone payment upon the dosing of the second patient in a clinical trial with the initial product candidate. The $7.0 million upfront payment combined with the recognition of deferred revenues resulted in a total to $30.3 million of revenue recognized in conjunction with the delivery of co-exclusive licenses to develop and commercialize various hemoglobinopathy targets under the JDA with Vertex. The net profits and net losses, as applicable, incurred under the JDA will be shared equally between us and Vertex.

Joint Venture Agreement- Casebia

In December 2015, we entered into an agreement, the JV Agreement, with Bayer HealthCare to create a joint venture, Casebia Therapeutics LLP, ("Casebia" or the "JV"), to discover, develop and commercialize CRISPR/Cas9 gene-editing therapeutics to treat the genetic causes of bleeding disorders, autoimmune disease, blindness, hearing loss and heart disease. We and Bayer HealthCare each have a 50% interest in the JV. Under the JV Agreement, Bayer HealthCare is making available its protein engineering expertise and relevant disease know-how and we are contributing our proprietary CRISPR/Cas9 gene editing technology and intellectual property. Bayer HealthCare will also provide up to $300.0 million in research and development investments to the JV over the first five years, subject to specified conditions.

In connection with the JV Agreement, the JV was required to pay us an aggregate amount of $35.0 million technology access fee, consisting of an upfront payment of $20.0 million, which was paid at the closing of the JV Agreement in March 2016, and another payment of $15.0 million for specified intellectual property rights relating to our CRISPR/Cas9 technology outside of the United States, which was paid in December 2016. In January 2016, we also issued a convertible loan to Bayer BV (the "Bayer Convertible Loan") for gross proceeds of $35.0 million which was immediately converted to Series B Preferred Shares at a conversion price of $13.43 per share. Concurrent with the IPO in October 2016, we issued and sold 2,500,000 common shares to Bayer BV, at the IPO price of $14.00 per share resulting in aggregate net proceeds of $35.0 million.

Financial Overview

Revenue

We have not generated any revenue to date from product sales and do not expect to do so in the near future. During the year ended December 31, 2017, 2016 and 2015 we recognized $41.0 million, $5.2 million, and $0.2 million, respectively, of revenue related to our collaboration agreements with Vertex and Casebia. We did not recognize any revenue during the year ended December 31, 2014. As of December 31, 2017, we had not received any milestone or royalty payments under the Vertex collaboration agreement. For additional information about our revenue recognition policy, see the "Critical Accounting Policies and Estimates—*Revenue*."

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our product discovery efforts and the development of our product candidates, which include:

- employee-related expenses, including salaries, benefits and equity-based compensation expense;
- costs of services 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 and other payments related to acquiring and maintaining licenses under our third-party licensing agreements.

Research and development costs are expensed as incurred. Nonrefundable advance payments for research and development goods or services to be received in the future are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed. At this time, we cannot reasonably estimate or know the nature, timing or estimated costs of the efforts that will be necessary to complete the development of any product candidates we may identify and develop. This is due to the numerous risks and uncertainties associated with developing such product candidates, including the uncertainty of:

- successful completion of preclinical studies and Investigational New Drug-enabling studies;
- successful enrollment in, and completion of, clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity;
- launching commercial sales of the product, if and when approved, whether alone or in collaboration with others;

- acceptance of the product, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies and treatment options;
- a continued acceptable safety profile following approval;
- enforcing and defending intellectual property and proprietary rights and claims; and
- achieving desirable medicinal properties for the intended indications.

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

Except for activities we perform in connection with our collaborations with Vertex and Casebia, 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 current development programs progress and new programs are added.

General and Administrative Expenses

General and administrative expenses consist primarily of employee related expenses, including salaries, benefits, and equity-based compensation, for personnel in executive, finance, accounting, business development and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters, and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future to support continued research and development activities, potential commercialization of our product candidates and increased costs of operating as a public company. We anticipate increased costs associated with being a public company, including expenses related to services associated with maintaining compliance with exchange listing and SEC requirements, insurance costs and investor relations costs, the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses. We also anticipate increased expenses related to the reimbursements of third-party patent related expenses in connection with the ongoing interference proceeding with respect to certain of our in-licensed intellectual property.

Results of Operations

Comparison of Years Ended December 31, 2017, and 2016

The following table summarizes our results of operations for the years ended December 31, 2017 and 2016, together with the dollar change in those items:

	Years Ended December 31, 2017	Years Ended December 31, 2016	Period-to-Period Change
	(in thousands)		
Collaboration revenue	$ 40,997	$ 5,164	$ 35,833
Operating expenses:			
Research and development	69,800	42,238	27,562
General and administrative	35,845	31,056	4,789
Total operating expenses	105,645	73,294	32,351
Loss from operations	(64,648)	(68,130)	3,482
Other (expense) income, net	(1,960)	45,412	(47,372)
Net loss before provision for from income taxes	(66,608)	(22,718)	(43,890)
Provision for income taxes	(1,749)	(484)	(1,265)
Net loss	$ (68,357)	$ (23,202)	$ (45,155)

Collaboration Revenue

Collaboration revenue for the year ended December 31, 2017 was $41.0 million, compared to $5.2 million for the year ended December 31, 2016. The increase of $35.8 million was primarily due to $30.3 million of revenue recognized in conjunction with the delivery of co-exclusive licenses to develop and commercialize various hemoglobinopathy targets under the Collaboration Agreement with Vertex and in connection with the execution of the JDA with Vertex, an increase in research and development service revenue from the collaboration with Vertex of $32.2 million, and an increase in research and development service revenue of $3.6 million from a collaboration agreement with Casebia. During the year ended December 31, 2016, we recognized $4.0 million and $1.2 million of research and development service revenue related to the collaboration with Vertex and Casebia, respectively.

Research and Development Expenses

Research and development expenses for the year ended December 31, 2017 was $69.8 million, compared to $42.2 million for the year ended December 31, 2016. The increase of $27.6 million in research and development expenses was primarily attributable to approximately $3.9 million in increased facilities costs including rent and utilities, $11.1 million in increased research and development variable process and platform development costs, $8.5 million in increased research and development employee compensation costs, $4.0 million in increased stock-based compensation costs and $0.1 million in increased consulting and professional services.

General and Administrative Expenses

General and administrative expenses were $35.8 million for the year ended December 31, 2017, compared to $31.1 million for the year ended December 31, 2016. The increase of $4.8 million was primarily due to the following increases in expenses: $3.7 million of employee-related costs to support our overall growth and $2.7 million in facilities costs including rent and utilities, partially offset by a decreases of $1.6 million of intellectual property costs including related to prior year third-party costs to procure the issuance of patents in jurisdictions outside the United States and costs related to an interference proceeding with respect to our in-licensed intellectual property.

Other (Expense) Income, Net

Other (expense) income, net, was $2.0 million of expense for the year ended December 31, 2017, compared to $45.4 million of income for the year ended December 31, 2016. The decrease of $47.4 million was primarily due to a loss from the equity method investment of $1.8 million as a result of stock based compensation awards with Casebia employees and other expenses of $0.2 million during 2017 as compared to a $78.5 million gain recognized in connection with the formation of Casebia which equaled the value of cash consideration received from Casebia and the fair value of the Company's equity interest in Casebia as of the formation of the JV in 2016, combined with an $11.5 million gain recognized on extinguishment of convertible loans with Vertex, all of which was partially offset by $36.5 million in 2016 equity method losses, and $8.1 million of interest expense related to a convertible loan with Bayer.

Comparison of Years Ended December 31, 2016, and 2015

The following table summarizes our results of operations for the years ended December 31, 2016 and 2015, together with the dollar change in those items:

	Years Ended December 31, 2016	Years Ended December 31, 2015	Period-to-Period Change
	(in thousands)		
Collaboration revenue	$ 5,164	247	$ 4,917
Operating expenses:			
Research and development	42,238	12,573	29,665
General and administrative	31,056	13,403	17,653
Total operating expenses	73,294	25,976	47,318
Loss from operations	(68,130)	(25,729)	(42,401)
Other income (expense), net	45,412	(92)	45,504
Net loss before provision for income taxes	(22,718)	(25,821)	3,103
Provision for income taxes	(484)	(7)	(477)
Net loss	$ (23,202)	$ (25,828)	$ 2,626

Collaboration Revenue

Collaboration revenue for the year ended December 31, 2016 was $5.2 million, compared to $0.2 million for the year ended December 31, 2015. The increase of $5.0 million was primarily due to a full year's worth of research and development service revenue from the collaboration with Vertex of $4.0 million, and research and development service revenue of $1.2 million under a collaboration agreement with Casebia. During the year ended December 31, 2015, we recognized $0.2 million of research and development service revenue related to the collaboration with Vertex.

Research and Development Expenses

Research and development expenses for the year ended December 31, 2016 was $42.2 million, compared to $12.6 million for the year ended December 31, 2015. The increase of $29.7 million in research and development expenses was primarily attributable to approximately $10.6 million in increased facilities costs including rent and utilities, $9.0 million in increased research and development variable process and platform development costs, $10.4 million in increased research and development employee compensation costs, partially offset by a $0.4 million reduction of license fees and consulting expenses.

General and Administrative Expenses

General and administrative expenses were $31.1 million for the year ended December 31, 2016, compared to $13.4 million for the year ended December 31, 2015. The increase of $17.7 million was primarily due to the following increases in expenses: $8.5 million of employee-related costs to support our overall growth; $3.9 million of intellectual property costs including third-party costs to procure the issuance of patents in jurisdictions outside the United States and costs related to an interference proceeding with respect to our in-licensed intellectual property, $2.0 million in non-recurring shareholder PFIC settlements, $1.1 million in facilities costs including rent and utilities, $1.6 million in capital and franchise taxes related to financing rounds, and $0.5 million of professional and consulting fees to support the requirements of being a public company.

Other Income (Expense), Net

Other income (expense), net, was $45.4 million of income for the year ended December 31, 2016, compared to $0.1 million of expense for the year ended December 31, 2015. The increase of $45.5 million was primarily due to a $78.6 million gain recognized in connection with the formation of Casebia which equaled the value of cash consideration received from Casebia and the fair value of the Company's equity interest in Casebia as of the formation of the JV, combined with an $11.5 million gain recognized on extinguishment of convertible loans with Vertex, all of which was partially offset by $36.5 million in 2016 equity method losses, and $8.1 million of interest expense related to a convertible loan with Bayer.

Liquidity and Capital Resources

As of December 31, 2017, we had cash and cash equivalents of approximately $239.8 million. In January 2018, the Company completed an offering of 5,750,000 shares of common, which were sold at a price of $22.75 per share. This offering resulted in $122.6 million of net proceeds to the Company. The underwriting discount of $7.8 million and other expenses of $0.4 million related to the equity offering were recorded as an offset to additional paid-in capital. With our cash on hand as of December 31, 2017 and the proceeds from the January 2018 offering, we expect cash and cash equivalents to be sufficient to fund its current operating plan through at least the next 24 months. As of December 31, 2017, our funds were held in non-interest-bearing deposit accounts.

We have incurred losses and cumulative negative cash flows from operations since our inception, and as of December 31, 2017, we had an accumulated deficit of $125.4 million. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may raise through public or private equity or debt financings, strategic collaborations, or other sources.

Funding Requirements

Our primary uses of capital are, and we expect will continue to be, research and development activities, compensation and related expenses, laboratory and related supplies, legal and other regulatory expenses, patent prosecution filing and maintenance costs for our licensed intellectual property and general overhead costs. We expect our expenses to increase compared to prior periods in connection with our ongoing activities, particularly as we continue research and development and preclinical activities, initiate preclinical studies to support initial drug applications. In addition, we expect to incur additional costs associated with operating as a public company.

Because our research programs are still in preclinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of any future product candidates or whether, or when, we may achieve profitability. Until such time as we can generate substantial product revenues, if ever, we expect to finance our cash needs through a combination of equity or debt financings and collaboration arrangements. We are entitled to research payments under our collaboration with Vertex. Additionally, we are eligible to earn payments, in each case, on a per-product basis under the JV Agreement with Bayer and our Collaboration Agreement and JDA with Vertex. Except for these sources of funding, we do not have any committed external source of liquidity. To the extent that we raise additional capital through the future sale of equity or debt securities, the ownership interest of our shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing shareholders. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Outlook

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect our existing cash and the proceeds from the January 2018 offering, will enable us to fund our operating expenses and capital expenditures for at least the next 24 months, without giving effect to any additional proceeds we may receive under our Collaboration Agreement and JDA with Vertex and the JV with Casebia. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Given our need for additional financing to support the long term clinical development of our programs, we intend to consider additional financing opportunities when market terms are favorable to us.

Our ability to generate revenue and achieve profitability depends significantly on our success in many areas, including: developing our delivery technologies and our CRISPR/Cas9 technology platform; selecting appropriate product candidates to develop; completing research and clinical and preclinical development of selected product candidates; obtaining regulatory approvals and marketing authorizations for product candidates for which we complete clinical trials; developing a sustainable and scalable manufacturing process for product candidates; launching and commercializing product candidates for which we obtain regulatory approvals and marketing authorizations, either directly or with a collaborator or distributor; obtaining market acceptance of our product candidates; addressing any competing technological and market developments; negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter; maintaining good relationships with our collaborators and licensors; maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and attracting, hiring and retaining qualified personnel.

Sources of Liquidity

Cash Flows

The following table provides information regarding our cash flows for each of the periods below:

	Years Ended December 31,		
	2017	2016	2015
		(in thousands)	
Net cash (used in) provided by operating activities	$ (70,097)	$ (55,310)	$ 59,428
Net cash (used in) provided by investing activities	(8,314)	31,884	(1,154)
Net cash provided by financing activities	2,608	183,220	96,733
Effect of exchange rate changes on cash	41	(235)	9
Net (decrease) increase in cash and cash equivalents	$ (75,762)	$ 159,559	$ 155,016

Net Cash (Used in) Provided by Operating Activities

Net cash used in operating activities was $70.1 million for the year ended December 31, 2017 and primarily consisted of a net loss of $68.4 million adjusted for non-cash items (including equity-based compensation expense of $18.9 million, depreciation and amortization expense of $3.0 million and a loss from equity method investment of $1.8 million), an increase in prepaid expenses and other current assets of $4.1 million, a decrease in accounts payable and accrued expenses of $0.8 million, a decrease in deferred revenue of $20.7 million and a decrease in deferred rent of $0.5 million, partially offset by a decrease of $0.5 million in accounts receivable and an increase in other liabilities of $0.3 million.

Net cash used in operating activities was $55.3 million for the year ended December 31, 2016 and primarily consisted of a net loss of $23.2 million adjusted for non-cash items (including equity-based compensation expense of $10.8 million, non-cash interest expense of $8.1 million, depreciation and amortization expense of $0.9 million, loss from equity method investment of $36.4 million, other income of $78.6 million recognized in connection with the formation of our JV with Bayer HealthCare, and a gain on extinguishment of the Vertex convertible loan of $11.5 million), an increase in prepaid expenses and other current assets of $1.1 million, and an increase in accounts receivable of $2.8 million, and an increase in restricted cash of $2.5 million, partially offset by an increase in accounts payable and accrued expenses of $3.9 million, deferred revenue of $1.9 million, and deferred rent of $2.4 million.

The net cash provided by operating activities was $59.4 million for the year ended December 31, 2015, and consisted primarily of a net loss of $25.8 million adjusted for non-cash items (including equity-based compensation expense of $3.7 million), depreciation of $0.1 million, along with an increase in prepaid expenses and other assets of $1.0 million and an increase of restricted cash of $0.7 million, offset by an increase in accounts payable and accrued expenses of $7.7 million, deferred revenue of $75.1 million, and deferred rent of $0.2 million.

Net Cash (Used in) Provided by Investing Activities

Net cash provided by investing activities for the year ended December 31, 2017 was $8.3 million and consisted primarily of purchases of property and equipment for use in research and development activities and leasehold improvements for our Cambridge, MA office.

Net cash provided by investing activities for the year ended December 31, 2016 was $31.9 million and consisted primarily of consisted of proceeds of $35.0 million from our contribution of intellectual property to the JV, offset by our contributions to the JV of $0.1 million, and the purchase of property and equipment of $3.0 million primarily associated with the commencement of internal research and development.

Net cash used in investing activities was $1.2 million during the year ended December 31, 2015, which resulted solely from the purchase of property and equipment primarily associated with the commencement of internal research and development operations in Cambridge, Massachusetts.

Net Cash Provided by Financing Activities

Net Cash provided by financing activities for the year ended December 31, 2017 was $2.6 million and consisted entirely of net proceeds from stock option exercises.

Net Cash provided by financing activities for the year ended December 31, 2016 was $183.2 million and consisted of net proceeds of $54.1 million from the issuance of common shares in the IPO, proceeds of $35.0 million from the issuance of common shares in a private placement with Bayer, gross proceeds of $22.9 million from the issuance of Series A-3 preferred shares, gross proceeds of $38.1 million from the issuance of Series B preferred shares and $35.0 million in proceeds from the issuance of a convertible loan to Bayer, offset by the issuance costs on preferred share financings of $1.8 million.

Net cash provided by financing activities was $96.7 million for the year ended December 31, 2015. The cash provided by financing activities for the year ended December 31, 2015 primarily consisted of net proceeds of $5.3 million related to a subscription receivable for Series A-2 Preferred Shares, $22.9 million from the issuance of Series A-3 Preferred Shares, $30.5 million from the issuance of Series B Preferred Shares and $38.2 million from the issuance of a convertible loan with Vertex and certain existing shareholders.

Contractual Obligations

The following table summarizes our significant contractual obligations as of payment due date by period at December 31, 2017 (in thousands):

	Year 1	Year 2-3	More than 3 Years	Total
Operating lease and sublease commitments	$ 4,908	$ 13,192	$ 37,396	$ 55,496

We enter into agreements in the normal course of business with vendors for preclinical research studies and other services and products for operating purposes.

Under the Invention Management Agreement ("IMA") signed on December 15, 2016, the Company is obligated to share costs related to patent maintenance, defense and prosecution for the CRISPR/Cas9 gene editing intellectual property with California, Vienna and their licensees including Caribou Biosciences, Inc. and Caribou's licensee Intellia Therapeutics, Inc.

Off-Balance Sheet Arrangements

As of December 31, 2017, we do not have any off-balance sheet arrangements, as defined under applicable SEC rules.

Critical Accounting Policies and Significant Judgments and Estimates

This discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. We believe that several accounting policies are important to understanding our historical and future performance. We refer to these policies as critical because these specific areas generally require us to make judgments and estimates about matters that are uncertain at the time we make the estimate, and different estimates—which also would have been reasonable—could have been used. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and other market-specific or other relevant assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements included elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Revenue

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

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

The Company records the elements of its collaboration agreements that represent joint operating activities in accordance with FASB ASC Topic 808, Collaborative Arrangements ("ASC 808"). Accordingly, the elements of the collaboration agreements that represent activities in which both parties are active participants and to which both parties are exposed to the significant risks and rewards that are dependent on the commercial success of the activities, are recorded as collaborative arrangements. The Company considers the guidance in FASB ASC Topic 605-45, Revenue Recognition—Principal Agent Considerations ("ASC 605-45") in determining the appropriate treatment for the transactions between the Company and its collaborative partner and the transactions between the Company and third parties. Generally, the classification of transactions under the collaborative arrangements is determined based on the nature and contractual terms of the arrangement along with the nature of the operations of the participants.

Multiple Element Arrangements

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

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

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

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

Recognition of Milestones and Royalties

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

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

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

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

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

Variable Interest Entities

We review each legal entity formed by parties related to the Company to determine whether or not the entity is a Variable Interest Entity, or VIE, in accordance with the Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 810, Consolidation. If the entity is a VIE, we assess whether or not we are the primary beneficiary of that VIE based on a number of factors, including (i) which party has the power to direct the activities that most significantly affect the VIE's economic performance, (ii) the parties' contractual rights and responsibilities pursuant to any contractual agreements and (iii) which party has the obligation to absorb losses or the right to receive benefits from the VIE. If we determine that we are the primary beneficiary of a VIE, we treat the VIE as a business combination and consolidate the financial statements of the VIE into our consolidated financial statements at the time that determination is made. On a quarterly basis, we evaluate whether it continues to be the primary beneficiary of any consolidated VIEs. If we determine that we are no longer the primary beneficiary of a consolidated VIE, or no longer have a variable interest in the VIE, we deconsolidate the VIE in the period that the determination is made.

If we determine that we are the primary beneficiary of a VIE that meets the definition of a business, we measure the assets, liabilities and non-controlling interests of the newly consolidated entity at fair value in accordance with FASB ASC Topic 805, Business Combinations on the date we become the primary beneficiary.

In February 2016, Casebia Therapeutics LLP, a limited liability partnership, was formed in the United Kingdom. In March 2016 upon consummation of the JV, we and Bayer each received a 50% equity interest in the entity in exchange for our contributions to the entity. We determined that Casebia was considered a VIE and concluded that we are not the primary beneficiary of the VIE. As such, we did not consolidate Casebia's results into the consolidated financial statements. We account for our 50% investment share of Casebia under the equity method of accounting. The formation of Casebia was accounted for at fair value. See Note 9 to the consolidated financial statements for further details relating to the evaluation of Casebia as a VIE as well as our accounting for the formation.

Equity-Based Compensation

We recognize equity-based compensation expense for awards of equity instruments to employees and non-employee directors based on the grant date fair value of those awards in accordance with FASB ASC Topic 718, Stock Compensation, or ASC 718. ASC 718 requires all equity-based compensation awards to employees and non-employee directors, including grants of restricted shares and stock options, to be recognized as expense in the statements of operations based on their grant date fair values. We estimate the fair value of stock options using the Black-Scholes option pricing model. We use the fair value of its Common Shares to determine the fair value of restricted share awards.

We account for stock options issued to non-employees and employees of Casebia under FASB ASC Topic 505-50, Equity Based Payments to Non-Employees, or ASC 505-50. As such, the value of such options is periodically remeasured, and income or expense is recognized over their vesting terms. Compensation cost related to awards with service-based vesting schedules is recognized using the straight-line method.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (i) the expected share price volatility, (ii) the calculation of expected term of the award, (iii) the risk-free interest rate and (iv) the expected dividend yield. Due to the lack of a public market for the trading of our Common Shares prior to its IPO and a lack of company-specific historical and implied volatility data, we based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The group of representative companies have characteristics similar to us, including stage of product development and focus on the life science industry. We use the simplified method, which is the average of the final vesting tranche date and the contractual term, to calculate the expected term for options granted to employees as it 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, we utilize the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is 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 has no current plans to pay any dividends on its Common Shares.

We expense the fair value of its equity-based compensation awards granted to employees with only service-based vesting on a straight-line basis over the associated service period, which is generally the period in which the related services are received. We measure equity-based compensation awards granted to non-employees at fair value as the awards vest and recognizes the resulting value as compensation expense at each financial reporting period.

We record the expense for equity-based compensation awards subject to performance-based milestone vesting over the remaining service period when management determines that achievement of the milestone is probable. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date. There have only been nine such awards to date.

The Company uses a Monte Carlo simulation option-pricing model to determine the fair value of market-based awards. The model uses the same input assumptions as the Black-Scholes model, yet, it also incorporates the possibility that the market condition may not be satisfied. Compensation cost related market-based awards are recognized regardless of whether the market condition is satisfied, provided that the requisite service has been provided.

Recent Accounting Pronouncements

Refer to Note 2, "Summary of Significant Accounting Policies," in the accompanying notes to the consolidated financial statements for a discussion of recent accounting pronouncements. On January 1, 2018, we adopted FASB issued Accounting Standards Update, or ASU, No. 2014-09, *Revenue from Contracts with Customers (Topic 606).* This standard replaces existing revenue recognition rules with a comprehensive revenue measurement and recognition standard and expanded disclosure requirements. See Note 2 of the consolidated financial statements for further discussion of the impact of the recently issued accounting standard.

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

Foreign Exchange Market Risk

As a result of our foreign operations, we face exposure to movements in foreign currency exchange rates, primarily the Swiss Franc and British Pound, against the U.S. dollar. The current exposures arise primarily from cash, accounts payable, and intercompany receivables and payables. Changes in foreign exchange rates affect our consolidated statement of operations and distort comparisons between periods. We do not engage in any foreign exchange rate hedging activities and therefore we are subject to foreign currency impacts.

Taxation

We are subject to corporate taxation in Switzerland.

Under Swiss law, we are entitled to carry forward losses we incur for a period of seven years and we can offset future profits, if any, against such losses. As of December 31, 2017, we reported tax loss carry forwards from inception through 2017 for purposes of Swiss federal direct taxes in the aggregate amount of CHF 103.1 million (including the loss incurred in 2017). As we have moved our legal seat from the Canton of Basel-Stadt to the Canton of Zug mid of 2017, it will be the Canton of Zug, which is in charge for assessing our tax return including our carry forward losses (to be noted that there will be a pro-rata allocation between the Canton of Basel-Stadt and Zug for capital tax purposes in 2017). No ruling regarding taxation as a mixed company has been filed with the Zug tax authorities; however, based on the practice of the Canton of Zug, we can apply for taxation as a mixed company in the tax return as long as the respective law is in force and we fulfill the respective criteria. According to the practice of the Canton of Zug and deviating from the tax rules of the Canton of Basel-Stadt a mixed company profit allocation is only performed once the company is profit making. Therefore, the tax loss carry forwards at cantonal level are the same as at federal level and therefore amount to some CHF 103.1 million in aggregate as of December 31. 2017. It is to be noted in this regard that tax losses are only finally assessed by the tax authorities when offset with taxable profit (which will not be the case as long we are loss making). If not used, these tax losses will expire seven years after the year in which they occurred. Due to our limited income, there is a high risk that the tax loss carry forwards will expire partly or entirely. For 2017, the tax return has – in accordance with Swiss tax law – not yet been filed. Therefore, for 2017 the loss carried forward will only be claimed with filing of the tax return for the tax year 2017.

The statutory corporate profit tax rate in the Canton of Basel-Stadt where we were domiciled (until mid-year 2017) amounted (federal and cantonal) to a maximum of 28.5% on the profit after tax (taxes are deductible). We applied for a tax privilege as a mixed company in the Canton of Basel-Stadt for the years 2013/2014, 2015 and ongoing years. This application was confirmed in February 2017. According to the ruling confirmation, the corporate profit tax rate as mixed company amounts to 11.5% (federal and cantonal) on the profit after tax. As already mentioned above, no tax ruling was filed with the Zug tax authorities, but as long as the respective law is in force and we fulfill the criteria, a respective application for taxation as a mixed company can be made in the annual tax return and will be granted by the Zug tax authorities. The statutory corporate profit tax rate (on the profit after tax) as mixed company in the Canton of Zug ranges between 9.36% and 10.65% on the profit after taxes (taxes are deductible), depending on the number of full time equivalents employed in Switzerland in a given year. The maximum tax rate applies in case we employ more than 30 full time equivalents by the end of a given year. The Canton does from time to time amend the level of taxation levied on corporations and there is no certainty that the tax rate currently in effect will not change in the future.

The privileges for mixed companies are under pressure and new tax legislations abolish mixed companies but at the same time lowering the ordinary tax rate is in preparation (e.g. the Canton of Zug has announced a planned reduction of its effective income tax rate to 12-12.5% (federal and cantonal)). Following the negative outcome of a revised tax legislation by a public vote on February 12, 2017, the scope and timing of such new tax legislation is uncertain, but currently expected for approx. 2020.

Item 8. Financial Statements and Supplementary Data.

The consolidated financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found in Item 15.

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

We maintain “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission’s rules and forms and (2) accumulated and communicated to our management, including our principal executive and principal financial officer, 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. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2017. Based upon such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2017, our disclosure controls and procedures were effective at the reasonable assurance level.

Management’s Annual Report on Internal Controls Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) of 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 U.S. generally accepted accounting principles, or GAAP. Our internal control over financial reporting includes those policies and procedures that: (i) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets, (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors, and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements. Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective.

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.

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 as of December 31, 2017 based on the criteria established in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework), or COSO. Based on our evaluation under the criteria set forth in Internal Control - Integrated Framework issued by the COSO, our management concluded our internal control over financial reporting was effective as of December 31, 2017.

Attestation Report of the Registered Public Accounting Firm

This Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the period covered by this Annual Report on Form 10-K that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

On March 7, 2018, the Board of Directors of the Company approved the payout of annual incentive compensation to our executive officers, based upon the over-achievement of corporate objectives set forth for 2017. Payout in excess of 100% was approved as follows: Rodger Novak - $258,530; Samarth Kulkarni - $196,264; Michael Tomsicek - $23,987 based on partial year employment.

In addition, on March 7th, 2018 the Board of Directors also approved a senior executive cash incentive plan (the "cash Bonus Plan"). The Cash Bonus Plan is designed to motivate, retain and reward the Company's executive officers based on the achievement of both individual objectives and corporate objectives established each year by the Board of Directors and/or the Compensation Committee therein.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item is incorporated by reference to our Proxy Statement for our 2018 Annual General Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2017.

Item 11. Executive Compensation.

The information required by this item is incorporated by reference to our Proxy Statement for our 2018 Annual General Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2017.

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

The information required by this item is incorporated by reference to our Proxy Statement for our 2018 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2017.

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

The information required by this item is incorporated by reference to our Proxy Statement for our 2018 Annual General Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2017.

Item 14. Principal Accounting Fees and Services.

The information required by this item is incorporated by reference to our Proxy Statement for our 2018 Annual General Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2017.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a)(1) Financial Statements.

See the "Index to Consolidated Financial Statements" on page F-1 below for the list of financial statements filed as part of this report.

(a)(2) Financial Statement Schedules.

I. Financial Statements of Casebia Therapeutics LLP (financial statements required by Regulation S-X).

Schedules other than that listed above have been omitted because of the absence of conditions under which they are required or because the required information is included in the financial statements or the notes thereto.

(a)(3) Exhibits.

The exhibits listed in the Exhibit Index below are filed or incorporated by reference as part of this Annual Report on Form 10-K.

Exhibit Index

Exhibit Number	Description
3.1	Amendment and Restated Articles of Association (incorporated herein by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on July 25, 2017).
4.1	Subscription Agreement, dated December 19, 2015, by and between CRISPR Therapeutics AG and Bayer Global Investments B.V. (incorporated herein by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1 filed on September 9, 2016).
10.1†	Joint Venture Agreement, dated December 19, 2015, between CRISPR Therapeutics AG and Bayer HealthCare LLC (incorporated herein by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1 filed on October 7, 2016).
10.2†	IP Contribution Agreement, dated March 16, 2016, by and between CRISPR Therapeutics AG, Bayer HealthCare LLC and Casebia Therapeutics LLP (incorporated herein by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1 filed on October 7, 2016).
10.3†	Option Agreement, dated March 16, 2016, by and between CRISPR Therapeutics AG, Bayer HealthCare LLC and Casebia Therapeutics LLP (incorporated herein by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 filed on October 7, 2016).
10.4†	Strategic Collaboration, Option and License Agreement, dated October 26, 2015, by and among CRISPR Therapeutics AG, CRISPR Therapeutics Limited, CRISPR Therapeutics, Inc., TRACR Hematology Limited, Vertex Pharmaceuticals, Incorporated and Vertex Pharmaceuticals (Europe) Limited (incorporated herein by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 filed on October 7, 2016).
10.5†	License Agreement, dated April 15, 2014, by and between CRISPR Therapeutics AG and Emmanuelle Marie Charpentier (incorporated herein by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 filed on October 7, 2016).
10.6†	License Agreement, dated April 15, 2014, by and between TRACR Hematology Limited and Emmanuelle Marie Charpentier (incorporated herein by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 filed on October 7, 2016).
10.7†	Patent Assignment Agreement, dated November 7, 2014, by and between CRISPR Therapeutics AG, Emmanuelle Marie Charpentier, the University of Vienna and Ines Fonfara (incorporated herein by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 filed on October 7, 2016).

Exhibit Number	Description
10.8	Form of Indemnification Agreement (incorporated herein by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 filed on October 7, 2016).
10.9	Registration Rights Agreement, dated June 10, 2016, by and among CRISPR Therapeutics AG and certain shareholders (incorporated herein by reference to Exhibit 10.9 to the Company's Registration Statement on Form S-1 filed on September 9, 2016).
10.10#	Employment Agreement, dated October 6, 2016, by and between CRISPR Therapeutics AG and Rodger Novak (incorporated herein by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 filed on October 7, 2016).
10.11#	Employment Agreement, effective December 1, 2017, by and between CRISPR Therapeutics AG and Rodger Novak (incorporated herein by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on December 21, 2017).
10.12#	Second Amended and Restated Employment Agreement, dated October 2, 2017, by and between CRISPR Therapeutics, Inc. and Samarth Kulkarni (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on October 2, 2017).
10.13#*	Employment Agreement, dated November 13, 2017, by and between CRISPR Therapeutics, Inc. and Michael Tomsicek.
10.14#	Amended and Restated Employment Agreement, dated October 6, 2016, by and between CRISPR Therapeutics, Inc. and Sven Ante Lundberg (incorporated herein by reference to Exhibit 10.13 to the Company's Registration Statement on Form S-1 filed on October 7, 2016).
10.15#	Advisory Agreement, dated December 20, 2017, by and between CRISPR Therapeutics, AG and Dr. Anthony Coles (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 21, 2017).
10.16#*	Employment Agreement, dated May 31, 2017, by and between CRISPR Therapeutics, Inc. and James R. Kasinger.
10.17#*	Employment Agreement, dated August 1, 2017, by and between CRISPR Therapeutics, Inc. and Tony Ho.
10.18#	CRISPR Therapeutics AG 2015 Stock Option and Grant Plan (incorporated herein by reference to Exhibit 10.14 to the Company's Registration Statement on Form S-1 filed on September 9, 2016).
10.19#	CRISPR Therapeutics AG Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on June 2, 2017).
10.19.1#	Form of Incentive Stock Option Agreement under CRISPR Therapeutics AG's Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.2 to the Company's Current Report on Form 10-Q filed on November 8, 2017).
10.19.2#	Form of Non-Qualified Stock Option Agreement for Company Employees under CRISPR Therapeutics AG's Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.3 to the Company's Current Report on Form 10-Q filed on November 8, 2017).
10.19.3#	Form of Non-Qualified Stock Option Agreement for Non-Employee Directors under CRISPR Therapeutics AG's Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.4 to the Company's Current Report on Form 10-Q filed on November 8, 2017).
10.19.4#	Form of Restricted Stock Award Agreement under CRISPR Therapeutics AG's Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.5 to the Company's Current Report on Form 10-Q filed on November 8, 2017).
10.19.5#	Form of Restricted Stock Award Agreement for Company Employees under CRISPR Therapeutics AG's Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.6 to the Company's Current Report on Form 10-Q filed on November 8, 2017).

Exhibit Number	Description
10.19.6#	Form of Restricted Stock Award Agreement for Non-Employee Directors under CRISPR Therapeutics AG's Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.7 to the Company's Current Report on Form 10-Q filed on November 8, 2017).
10.20#*	CRISPR Therapeutics AG 2018 Stock Option and Incentive Plan.
10.20.1#*	Form of Incentive Stock Option Agreement under CRISPR Therapeutics AG's 2018 Stock Option and Incentive Plan.
10.20.2#*	Form of Non-Qualified Stock Option Agreement for Company Employees under CRISPR Therapeutics AG's 2018 Stock Option and Incentive Plan.
10.20.3#*	Form of Non-Qualified Stock Option Agreement for Non-Employee Directors under CRISPR Therapeutics AG's 2018 Stock Option and Incentive Plan.
10.20.4#*	Form of Restricted Stock Award Agreement under CRISPR Therapeutics AG's 2018 Stock Option and Incentive Plan.
10.20.5#*	Form of Restricted Stock Award Agreement for Company Employees under CRISPR Therapeutics AG's 2018 Stock Option and Incentive Plan.
10.20.6#*	Form of Restricted Stock Award Agreement for Non-Employee Directors under CRISPR Therapeutics AG's 2018 Stock Option and Incentive Plan.
10.21#	CRISPR Therapeutics AG 2016 Employee Stock Purchase Plan (incorporated herein by reference to Exhibit 10.16 to the Company's Registration Statement on Form S-1 filed on September 9, 2016).
10.22	Consent to Sublease, dated May 16, 2016, by and between CRISPR Therapeutics, Inc and Pfizer Inc. (incorporated herein by reference to Exhibit 10.17 to the Company's Registration Statement on Form S-1 filed on September 9, 2016).
10.23†	Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement for a Programmable DNA Restriction Enzyme for Genome Editing, dated December 15, 2016, by and among CRISPR Therapeutics AG, The Regents of the University of California, University of Vienna, Dr. Emmanuelle Charpentier, Intellia Therapeutics, Inc., Caribou Biosciences, Inc., ERS Genomics Ltd., and TRACR Hematology Ltd. (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 16, 2016).
10.24†	Joint Development and Commercialization Agreement by and between, on the one hand, Vertex Pharmaceuticals Incorporated and Vertex Pharmaceuticals (Europe) Limited, and on the other hand, CRISPR Therapeutics AG, CRISPR Therapeutics, Inc., CRISPR Therapeutics Limited and TRACR Hematology Ltd., dated as of December 12, 2017 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 18, 2017).
10.25†	Amendment No. 1 to the Strategic Collaboration, Option and License Agreement by and between, on the one hand, Vertex Pharmaceuticals Incorporated and Vertex Pharmaceuticals (Europe) Limited, and on the other hand, CRISPR Therapeutics AG, CRISPR Therapeutics, Inc., CRISPR Therapeutics Limited and TRACR Hematology Ltd., dated as of December 12, 2017 (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on December 18, 2017).
10.26*	Senior Executive Cash Incentive Bonus Plan.
21.1*	Subsidiaries of the Registrant
23.1*	Consent of Ernst & Young LLP
23.2*	Consent of Ernst & Young LLP – Casebia Therapeutics, LLP
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.

Exhibit Number	Description
32.1+	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.
\+ Furnished herewith.
† Confidential treatment obtained as to certain portions.
\# A management contract or compensatory plan or arrangement required to be filed as an exhibit pursuant to Item 15(a)(3) of Form 10-K.

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, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

CRISPR Therapeutics AG

Date: March 8, 2018

By: /s/ Samarth Kulkarni
Samarth Kulkarni
Chief Executive Officer

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned directors and officers of CRISPR Therapeutics AG (the "Company"), hereby severally constitute and appoint Rodger Novak, Samarth Kulkarni, Michael Tomsicek and James R. Kasinger, and each of them singly, our true and lawful attorneys, with full power to them, and to each of them singly, to sign for us and in our names in the capacities indicated below, any and all amendments to this Annual Report on Form 10-K, and to file or cause to be filed the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as each of us might or could do in person, and hereby ratifying and confirming all that said attorneys, and each of them, or their substitute or substitutes, shall do or cause to be done by virtue of this Power of Attorney.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Samarth Kulkarni Samarth Kulkarni	Chief Executive Officer (Principal Executive Officer)	March 8, 2018
/s/ Michael Tomsicek Michael Tomsicek	Chief Financial Officer (Principal Financial and Accounting Officer)	March 8, 2018
/s/ Rodger Novak Rodger Novak	President and Director	March 8, 2018
/s/ Kurt Von Emster Kurt Von Emster	Director	March 8, 2018
/s/ Ali Behbahani Ali Behbahani	Director	March 8, 2018
/s/ Bradley Bolzon Bradley Bolzon	Director	March 8, 2018
/s/ Pablo Cagnoni Pablo Cagnoni	Director	March 8, 2018
/s/ Simeon J. George Simeon J. George	Director	March 8, 2018
/s/ Thomas Woiwode Thomas Woiwode	Director	March 8, 2018
/s/ Michael Tomsicek Michael Tomsicek	Authorized Representative in the United States	March 8, 2018

CRISPR Therapeutics AG

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of
CRISPR Therapeutics AG

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of CRISPR Therapeutics AG (the Company) as of December 31, 2017 and 2016, and the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred shares and shareholders' (deficit) equity, and cash flows for each of the three years in the period ended December 31, 2017 and the related notes (collectively referred to as the “financial statements”). In our opinion, the financial statements present fairly, in all material respects, the consolidated financial position of the Company at December 31, 2017 and 2016, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

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

CRISPR Therapeutics AG
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash	$ 239,758	$ 315,520
Accounts receivable, including related party amounts of $821 and $752 as of December 31, 2017 and 2016, respectively	2,626	3,157
Prepaid expenses and other current assets, including related party amounts of $1,871 and $0 as of December 31, 2017 and 2016, respectively	6,001	1,511
Total current assets	248,385	320,188
Property and equipment, net	18,857	21,027
Intangible assets, net	344	399
Restricted cash	3,154	3,150
Other non-current assets	606	198
Total assets	$ 271,346	$ 344,962
Liabilities, redeemable convertible preferred shares and shareholders' equity		
Current liabilities:		
Accounts payable	$ 1,639	$ 4,569
Accrued expenses, including related party amounts of $0 and $537 as of December 31, 2017 and 2016, respectively	11,361	16,320
Accrued tax liabilities	347	23
Deferred rent	1,027	1,027
Other current liabilities	137	59
Total current liabilities	14,511	21,998
Deferred revenue, including related party amounts of $91 and $527 as of December 31, 2017 and 2016, respectively	56,928	77,646
Deferred rent non-current	11,761	12,283
Other non-current liabilities	314	189
Total liabilities	83,514	112,116
Commitments and contingencies (Note 8)		
Shareholders' equity (deficit):		
Common shares, CHF 0.03 par value, 41,092,969 and 40,253,674 shares authorized at December 31, 2017 and 2016, respectively, 41,037,121 and 40,164,307 shares issued at December 31, 2017 and 2016, respectively, 40,592,248, and 39,719,434 shares outstanding at December 31, 2017 and 2016, respectively, 16,419,632 and 15,325,607 shares in conditional capital at December 31, 2017 and 2016, respectively.	1,240	1,216
Treasury shares, at cost, 444,873 shares and no shares at December 31, 2017 and 2016, respectively	—	—
Additional paid-in capital	312,018	288,739
Accumulated deficit	(125,440)	(57,083)
Accumulated other comprehensive income (loss)	14	(26)
Total shareholders' equity	187,832	232,846
Total liabilities and shareholders' equity	$ 271,346	$ 344,962

See accompanying notes to these consolidated financial statements.

CRISPR Therapeutics AG
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)

	Years Ended December 31, 2017	2016	2015
Collaboration revenue (1)	$ 40,997	$ 5,164	$ 247
Operating expenses:			
Research and development (2)	69,800	42,238	12,573
General and administrative	35,845	31,056	13,403
Total operating expenses	105,645	73,294	25,976
Loss from operations	(64,648)	(68,130)	(25,729)
Other (expense) income:			
Interest expense	—	(8,050)	(108)
Loss from equity method investment	(1,763)	(36,532)	—
Gain on extinguishment of convertible loan	—	11,482	—
Other (expense) income, net	(197)	78,512	16
Total other (expense) income, net	(1,960)	45,412	(92)
Net loss before provision for from income taxes	(66,608)	(22,718)	(25,821)
Provision for income taxes	(1,749)	(484)	(7)
Net loss	(68,357)	(23,202)	(25,828)
Foreign currency translation adjustment	40	(18)	(6)
Comprehensive loss	$ (68,317)	$ (23,220)	$ (25,834)
Reconciliation of net loss to net loss attributable to common shareholders:			
Net loss	$ (68,357)	$ (23,202)	$ (25,828)
Loss attributable to noncontrolling interest	—	25	325
Net loss attributable to common shareholders	$ (68,357)	$ (23,177)	$ (25,503)
Net loss per share attributable to common shareholders—basic and diluted	$ (1.71)	$ (1.89)	$ (5.06)
Weighted-average common shares outstanding used in net loss per share attributable to common shareholders—basic and diluted	40,057,365	12,257,483	5,037,404
(1) Including the following amounts of revenue from a related party, see Note 16:	$ 4,760	$ 1,190	$ —
(2) Including the following amounts of research and development from a related party, see Note 16:	$ 4,523	$ 1,755	$ 1,055

See accompanying notes to these consolidated financial statements.

CRISPR Therapeutics AG
Consolidated Statements of Redeemable Convertible Preferred Shares and Shareholders’ (Deficit) Equity
(In thousands, except share and per share data)

	Series A-1 Redeemable Convertible Preferred Shares		Series A-2 Redeemable Convertible Preferred Shares		Series A-3 Redeemable Convertible Preferred Shares		Series B Redeemable Convertible Preferred Shares		Common Shares		Treasury Shares							
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	CHF 0.03 Par Value	Shares	Amount, at cost	Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total CRISPR Therapeutics AG Shareholders’ (Deficit) Equity	Noncontrolling Interest	Total Shareholders’ (Deficit) Equity
Balance at December 31, 2014	440,001	$ 1,169	3,120,001	$ 5,101	—	$ —	—	$ —	3,559,985	$ 120	—	—	$ 1,168	$ (8,403)	$ (2)	$ (7,117)	$ 143	$ (6,974)
Receipt of Series A-2 preferred shares subscription receivable	—	—	—	5,293	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Issuance of Series A-3 preferred shares, net of issuance costs of $332 and subscription receivable of $22,850	—	—	—	—	10,758,006	22,518	—	—	—	—	—	—	—	—	—	—	—	—
Adjustment to noncontrolling interest upon share exchange transaction for TRACR Hematology Limited	—	—	—	—	—	—	—	—	1,968,094	61	—	—	1	—	—	62	(62)	—
Issuance of Series B preferred shares, net of issuance costs of $38	—	—	—	—	—	—	4,519,016	30,440	—	—	—	—	—	—	—	—	—	—
Equity-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	3,467	—	—	3,467	217	3,684
Other comprehensive income (loss)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(6)	(6)	—	(6)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	(25,503)	—	(25,503)	(325)	(25,828)
Balance at December 31, 2015	440,001	$ 1,169	3,120,001	$ 10,394	10,758,006	$ 22,518	4,519,016	$ 30,440	5,528,079	$ 181	—	—	$ 4,636	$ (33,906)	$ (8)	$ (29,097)	$ (27)	$ (29,124)
Conversion of Convertible Loans	—	—	—	—	—	—	5,464,608	61,929	—	—	—	—	—	—	—	—	—	—
Receipt of Series A-3 Subscription Receivable	—	—	—	—	—	22,850	—	—	—	—	—	—	—	—	—	—	—	—
Issuance of Series B Preferred Shares, net of issuance costs of $1.8 million	—	—	—	—	—	—	2,834,252	36,265	—	—	—	—	—	—	—	—	—	—
Conversion of redeemable convertible preferred shares into common share	(440,001)	(1,169)	(3,120,001)	(10,394)	(10,758,006)	(45,368)	(12,817,876)	(128,634)	27,135,884	823			184,742			185,565		185,565
Adjustment to Noncontrolling interest upon share exchange for TRACR	—	—	—	—	—	—	—	—	328,017	10			(62)			(52)	52	—
Issuance of common stock, net of issuance costs of $8.3 million	—	—	—	—	—	—	—	—	7,100,000	213			88,451			88,664		88,664
Repurchase of treasury shares	—	—	—	—	—	—	—	—	(444,873)	(13)	444,873	—	13	—	—	—	—	—
Vesting of restricted shares									53,427	1			81			82		82
Exercise of vested options	—	—	—	—	—	—	—	—	18,900	1	—	—	34	—	—	35	—	35
Stock- based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	10,844	—	—	10,844	—	10,844
Other comprehensive income (loss)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(18)	(18)	—	(18)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	(23,177)	—	(23,177)	(25)	(23,202)
Balance at December 31, 2016	—	$ —	—	$ —	—	$ —	—	$ —	39,719,434	$ 1,216	444,873	$ —	$ 288,739	$ (57,083)	$ (26)	$ 232,846	$ —	$ 232,846
Vesting of restricted shares							—	—	33,519	1	—	—	58	—	—	59	—	59
Exercise of vested options	—	—	—	—	—	—	—	—	839,295	23	—	—	2,585	—	—	2,608	—	2,608
Stock- based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	20,636	—	—	20,636	—	20,636
Other comprehensive income (loss)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	40	40	—	40
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	(68,357)	—	(68,357)	—	(68,357)
Balance at December 31, 2017	—	$ —	—	$ —	—	$ —	—	$ —	40,592,248	$ 1,240	444,873	$ —	$ 312,018	$ (125,440)	$ 14	$ 187,832	$ —	$ 187,832

See accompanying notes to these consolidated financial statements.

CRISPR Therapeutics AG
Consolidated Statements of Cash Flows
(In thousands)

	Years Ended December 31,		
	2017	2016	2015
Operating activities			
Net loss	$ (68,357)	$ (23,202)	$ (25,828)
Reconciliation of net loss to net cash used in operating activities:			
Depreciation and amortization	3,024	925	127
Equity-based compensation	18,873	10,844	3,684
Non-cash interest	—	8,050	97
Unrealized foreign currency remeasurement (gain) loss	(9)	2	(20)
Gain on extinguishment of convertible loan	—	(11,482)	—
Other income - formation of joint venture	—	(78,608)	—
Loss from equity method investment	1,763	36,380	—
Changes in:			
Restricted cash	(4)	(2,450)	(650)
Accounts receivable	531	(2,818)	(339)
Prepaid expenses and other assets	(4,117)	(1,071)	(620)
Accounts payable and accrued expenses	(831)	3,860	7,708
Deferred revenue	(20,718)	1,917	75,090
Deferred rent	(522)	2,360	165
Other liabilities, net	270	(17)	14
Net cash (used in) provided by operating activities	(70,097)	(55,310)	59,428
Investing activities			
Purchase of property and equipment	(7,814)	(3,016)	(1,154)
Proceeds from contribution of intellectual property to equity method investee	—	35,000	—
Cash investment in equity method investee	—	(100)	—
Purchase of available for sale debt security	(500)	—	—
Net cash (used in) provided by investing activities	(8,314)	31,884	(1,154)
Financing activities			
Proceeds from issuance of common shares in IPO, net of issuance costs	—	54,061	—
Proceeds from issuance of common shares in private placement	—	35,000	—
Proceeds from exercise of options	2,608	34	—
Proceeds from issuance of restricted shares	—	—	243
Proceeds from issuance of Series A-2 preferred shares	—	—	5,293
Proceeds from issuance of Series A-3 preferred shares	—	22,850	22,850
Proceeds from issuance of Series B preferred shares	—	38,075	30,478
Issuance costs for preferred share financings	—	(1,810)	(370)
Proceeds from issuance of convertible loans	—	35,010	38,239
Net cash provided by financing activities	2,608	183,220	96,733
Effect of exchange rate changes on cash	41	(235)	9
(Decrease) increase in cash	(75,762)	159,559	155,016
Cash, beginning of period	315,520	155,961	945
Cash, end of period	$ 239,758	$ 315,520	$ 155,961
Supplemental disclosure of non-cash investing and financing activities			
Property and equipment purchases in accounts payable and accrued expenses	$ —	$ 7,014	$ 246
Costs for proposed supplemental offering in accounts payable and accrued expenses	$ 290	$ —	$ —
Property and equipment related to lease incentives	$ —	$ 10,785	$ —
Conversion of preferred shares to common shares upon IPO	$ —	$ 185,565	$ —
Conversion of Vertex and Bayer convertible loans and accrued interest	$ —	$ 61,929	$ —
Issuance costs for public offering in accounts payable and accrued expenses	$	$ 397	$ —
Contribution of intellectual property to Casebia	$	$ 36,380	$ —

See accompanying notes to these consolidated financial statements.

1. Organization and Operations

Nature of business

CRISPR Therapeutics AG ("CRISPR" or the "Company") was formed on October 28, 2013 in Basel, Switzerland. In 2017, the Company changed its registered office to Zug, Switzerland. The Company was established to translate CRISPR/Cas9, a genome editing technology, into transformative gene-based medicines for the treatment of serious human diseases. The foundational intellectual property underlying the Company's operations was licensed to the Company and its subsidiaries in April 2014. The Company devotes substantially all of its efforts to product research and development activities, initial market development and raising capital. The Company's principal offices are headquartered in Zug, Switzerland and operations are in Cambridge, Massachusetts.

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.

The Company had an accumulated deficit of $125.4 million as of December 31, 2017 and has financed its operations to date from proceeds obtained from its initial public offering, a series of preferred shares and convertible loan issuances, and upfront fees received under its collaboration and joint venture arrangements. The Company will require substantial additional capital to fund its research and development and ongoing operating expenses.

Liquidity

In January 2018, the Company completed an offering of 5,750,000 shares of common shares, which were sold at a price of $22.75 per share. This offering resulted in $122.6 million of net proceeds to the Company. Refer to Note 17 "Subsequent Events" in the accompanying notes to the consolidated financial statements for further details regarding the January 2018 sale of common stock. The Company believes its cash of $239.8 million at December 31, 2017 and the proceeds from the January 2018 offering will be sufficient to fund the Company's current operating plan for at least the next 24 months. Thereafter, the Company will be required to obtain additional funding. There can be no assurances, however, that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all.

2. Summary of Significant Accounting Policies and basis of presentation

Basis of Presentation and Use of Estimates

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"), and include the accounts of (i) the Company, (ii) its wholly-owned subsidiaries, CRISPR Therapeutics Ltd., CRISPR Therapeutics Inc., and TRACR Hematology Inc., as of December 31, 2017. All intercompany accounts and transactions have been eliminated. 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 ("ASUs") of the Financial Accounting Standards Board ("FASB").

Investments in partnerships where the Company has significant influence because it has a voting interest of 20% to 50%, are accounted for under the equity method. Results of associated companies are presented on a one-line basis. The Company accounts for its 50% investment share of Casebia Therapeutics LLP ("Casebia") under the equity method of accounting. See Note 9 for further details.

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, equity-based compensation expense, revenue recognition, equity method investments, and reported amounts of expenses during the reported period. Significant estimates in these consolidated financial statements have been made in connection with the calculation of revenues, research and development expenses, valuation of equity method of investment, equity-based compensation expense, fair value of Common Shares, fair value of intangible assets, and the provision for or benefit from income taxes. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

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, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company and the Company's chief operating decision maker, namely, the chief executive officer, view the Company's operations and manage its business in one operating segment, which is the business of discovering, developing and commercializing therapies derived from or incorporating genome-editing technology.

Foreign Currency Translation and Transactions

The Company's reporting currency is the U.S. Dollar. The Company's consolidated entities have the U.S. dollar as their functional currency with the exception of CRISPR Ltd. which has the British Pound Sterling ("GBP") as its functional currency. CRISPR Ltd. has assets and liabilities translated into U.S. dollars at exchange rates in effect at the end of the year. Revenue and expenses are translated using the average exchange rates for the period. Net unrealized gains and losses resulting from foreign currency translation are included in accumulated other comprehensive income (loss), which is a separate component of shareholders' (deficit) equity. Net foreign currency exchange transaction gains and losses resulting from the remeasurement of transactions denominated in currencies other than functional currency are included in other (expense) income, net in the consolidated statements of operations and comprehensive loss.

Cash and Cash Equivalents

The Company considers all highly liquid investments with maturities of 90 days or less from the purchase date to be cash equivalents. As of December 31, 2017 and 2016, the Company had $239.8 million and $315.5 million in cash equivalents, respectively. All cash was held in depository accounts and is reported at fair value.

Accounts Receivable

Accounts receivable of $2.6 million at December 31, 2017 consist of receivables from Vertex Pharmaceuticals, Incorporated ("Vertex") and Casebia. As of December 31, 2016, the Company had accounts receivable of $3.2 million consisting of receivables from Vertex. Accounts receivables are recorded at invoiced amounts due under both the Vertex and Casebia collaboration agreements (see Note 9). Vertex and Casebia are creditworthy entities that maintain an ongoing relationship with the Company, as such the Company did not have an allowance for estimated losses recorded related to these receivables.

Concentrations of Credit Risk and Off-balance Sheet Risk

Financial instruments that potentially subject the Company to concentrations of credit risk are primarily cash. The Company's cash is held in accounts with financial institutions that management believes are creditworthy. 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. The Company has no financial instruments with off-balance sheet risk of loss.

Fair Value of Financial Instruments

The Company's financial instruments consist of a convertible debt instrument, accounts payable, accrued expenses and other non-current liabilities. The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. FASB ASC Topic 820, *Fair Value Measurement and Disclosures* ("ASC 820"), established a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available. Observable inputs are inputs that market participants would use in pricing the financial instrument 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 financial instrument and are developed based on the best information available in the circumstances.

The accounting standard describes a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value, which are the following:

Level 1 —Quoted prices in active markets that are accessible at the market date for identical unrestricted assets or liabilities.

Level 2 —Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs for which all significant inputs are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 —Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

To the extent that 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 amount of accounts receivable, accounts payable, and accrued expenses as reported on the consolidated balance sheets as of December 31, 2017 and 2016, approximate fair value, due to the short-term duration of these instruments.

The fair value of the Company's equity method investment in Casebia and convertible debt instruments were determined using level 3 inputs (See Note 9).

Property and Equipment

Property and equipment 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. Upon disposal, the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss is included in the results of operations. Depreciation is recorded using the straight-line method over the estimated useful lives of the respective assets, which are as follows:

Asset	Estimated useful life
Computer equipment	3 years
Furniture, fixtures, and other	5 years
Laboratory equipment	5 years
Leasehold improvements	Shorter of useful life or remaining lease term

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 value 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 value of the assets exceed their fair value. The Company has not recognized any impairment losses in the years ended December 31, 2017, 2016, and 2015.

Revenue Recognition

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

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

The Company records the elements of its collaboration agreements that represent joint operating activities in accordance with FASB ASC Topic 808, Collaborative Arrangements ("ASC 808"). Accordingly, the elements of the collaboration agreements that represent activities in which both parties are active participants and to which both parties are exposed to the significant risks and rewards that are dependent on the commercial success of the activities, are recorded as collaborative arrangements. The Company considers the guidance in FASB ASC Topic 605-45, Revenue Recognition—Principal Agent Considerations ("ASC 605-45") in determining the appropriate treatment for the transactions between the Company and its collaborative partner and the transactions between the Company and third parties. Generally, the classification of transactions under the collaborative arrangements is determined based on the nature and contractual terms of the arrangement along with the nature of the operations of the participants.

To date, the Company's only source of revenue has been the collaboration and license and joint development and commercialization agreement with Vertex as well as research and development services provided to Casebia under the joint venture with Bayer HealthCare LLC ("Bayer") (see Note 9).

The Company evaluates multiple-element arrangements based on the guidance in FASB ASC Topic 605-25, *Revenue Recognition—Multiple-Element Arrangements* ("ASC 605-25"). Pursuant to the guidance in ASC 605-25, the Company evaluates multiple-element arrangements to determine (i) the deliverables included in the arrangement and (ii) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. When deliverables are separable, consideration received is allocated to the separate units of accounting based on the relative selling price method and the appropriate revenue recognition principles are applied to each unit. When the Company determines that an arrangement should be accounted for as a single unit of accounting, the Company must determine the period over which the performance obligations will be performed and revenue will be recognized. This evaluation requires the Company to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that (i) the delivered item has value to the collaboration partner on a standalone basis and (ii) if the arrangement includes a general right of return with respect to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the Company's control. In assessing whether an item has standalone value, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can use any other deliverable for its intended purpose without the receipt of the remaining deliverable, whether the value of the deliverable is dependent on the undelivered item, and whether there are other vendors that can provide the undelivered items.

The consideration received under the arrangement that is fixed or determinable is then allocated among the separate units of accounting based on the relative selling prices of the separate units of accounting. The Company determines the selling price of a unit of accounting within each arrangement following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, the Company determines the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence ("VSOE") of selling price, if available; third-party evidence ("TPE") of selling price if VSOE is not available; or best estimate of selling price ("BESP") if neither VSOE nor TPE is available. The Company typically uses BESP to estimate the selling price as it generally does not have VSOE or TPE of selling price for its units of accounting. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company periodically validates the BESP used for units of accounting by evaluating whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

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

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

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

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

Research and Development Expenses

Research and development costs, which include employee compensation costs, facilities, lab supplies and materials, overhead, preclinical development, and other related costs, are charged to expense as incurred. Research and development costs also include the costs the Company incurs in its performance of services or provision of materials in connection with the funded research undertaken as a part of the Company's collaborative agreement with Vertex and Casebia. See Note 9 for further details.

Operating Leases

The Company leases office and laboratory facilities under a non-cancelable operating lease agreements. The lease agreements contain free or escalating rent payment provisions. The Company recognizes rent expense under such leases on a straight-line basis over the term of the lease with the difference between the expense and the payments recorded as deferred rent on the consolidated balance sheets. Lease renewal periods are considered on a lease-by-lease basis in determining the lease term. Funding of leasehold improvements by the Company's landlord are accounted for as a tenant improvement allowance and are amortized as a reduction of rent expense over the term of the lease. Leasehold improvements are amortized straight-line over the shorter of the useful life or the remaining lease term.

Equity Based Compensation Expense

The Company recognizes equity-based compensation expense for awards of equity instruments to employees and non-employee directors based on the grant date fair value of those awards in accordance with FASB ASC Topic 718, *Stock Compensation* ("ASC 718"). ASC 718 requires all equity-based compensation awards to employees and non-employee directors, including grants of restricted shares and stock options, to be recognized as expense in the statements of operations based on their grant date fair values. The Company estimates the fair value of stock options using the Black-Scholes option pricing model. The Company uses the fair value of its Common Shares to determine the fair value of restricted share awards. Certain equity awards include both time-based and market-based conditions and are accounted for as market-based awards. The fair value of these market-based awards is estimated on the date of grant using a Monte Carlo simulation model.

The Company accounts for stock options issued to non-employees under FASB ASC Topic 505-50, *Equity Based Payments to Non-Employees* ("ASC 505-50"). As such, the value of such options is periodically remeasured and income or expense is recognized over their vesting terms. Compensation cost related to awards with service-based vesting schedules is recognized using the straight-line method.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (i) the expected share price volatility, (ii) the calculation of expected term of the award, (iii) the risk-free interest rate and (iv) the expected dividend yield. Due to the lack of a public market for the trading of the Company's Common Shares prior to its IPO and a lack of company-specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The group of representative companies have characteristics similar to the Company, including stage of product development and focus on the life science industry. The Company uses the simplified method, which is the average of the final vesting tranche date and the contractual term, to calculate the expected term for options granted to employees as it 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 assumption. The risk-free interest rate is 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 has no current plans to pay any dividends on its Common Shares.

The Company expenses the fair value of its equity-based compensation awards granted to employees on a straight-line basis over the associated service period, which is generally the period in which the related services are received. The Company measures equity-based compensation awards granted to non-employees at fair value as the awards vest and recognizes the resulting value as compensation expense at each financial reporting period.

The Company records the expense for equity-based compensation awards subject to performance-based milestone vesting over the remaining service period using the accelerated method when management determines that achievement of the milestone is probable. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date.

The Company use a Monte Carlo simulation option-pricing model to determine the fair value of market-based awards. The model uses the same input assumptions as the Black-Scholes model, yet, it also incorporates the possibility that the market condition may not be satisfied. Compensation cost related to market-based awards are recognized using the accelerated method regardless of whether the market condition is satisfied, provided that the requisite service has been provided.

Patent Costs

Costs to secure and prosecute patent application and other legal costs related to the protection of the Company's intellectual property are expensed as incurred and are classified as general and administrative expenses in the Company's consolidated statements of operations.

Income Taxes

Income taxes are recorded in accordance with FASB 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 tax reporting basis of assets and liabilities and are measured using enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company has evaluated available evidence and concluded that the Company may not realize all the benefit of its deferred tax assets; therefore, a valuation allowance has been established for the amount of the deferred tax assets that the Company does not believe is more likely than not to be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes 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. As of December 31, 2017 and 2016, the Company does not have any significant uncertain tax positions. The Company's practice is to recognize interest and/or penalties related to income tax matters in income tax expense. See Note 14 for further details.

Comprehensive Loss

Comprehensive loss consists of net income or loss and changes in equity during the period from transactions and other events and circumstances generated from non-owner sources. The Company's net loss equals comprehensive loss, net of any changes in the foreign currency translation adjustment, for all periods presented. In addition, comprehensive loss attributable to the noncontrolling interest equals net loss for all periods presented.

Variable Interest Entities

The Company reviews each legal entity formed by parties related to the Company to determine whether or not the Company has a variable interest in the entity and whether or not the entity would meet the definition of a VIE in accordance with FASB ASC Topic 810, *Consolidation* ("ASC 810"). If the entity is a VIE, the Company assesses whether or not the Company is the primary beneficiary of that VIE based on a number of factors, including (i) which party has the power to direct the activities that most significantly affect the VIE's economic performance, (ii) the parties' contractual rights and responsibilities pursuant to any contractual agreements and

(iii) which party has the obligation to absorb losses or the right to receive benefits from the VIE. If the Company determines it is the primary beneficiary of a VIE, the Company consolidates the financial statements of the VIE into the Company's consolidated financial statements at the time that determination is made. The Company evaluates whether it continues to be the primary beneficiary of any consolidated VIEs on a quarterly basis. If the Company were to determine that it is no longer the primary beneficiary of a consolidated VIE, or no longer has a variable interest in the VIE, it would deconsolidate the VIE in the period that the determination is made.

If the Company determines it is the primary beneficiary of a VIE that meets the definition of a business, the Company measures the assets, liabilities and noncontrolling interests of the newly consolidated entity at fair value in accordance with FASB ASC Topic 805, *Business Combinations* ("ASC 805") at the date the reporting entity first becomes the primary beneficiary.

In February 2016, Casebia Therapeutics LLP, a limited liability partnership, was formed in the United Kingdom. In March 2016 upon consummation of the JV, Bayer and the Company each received a 50% equity interest in the entity in exchange for their contributions to the entity. The Company determined that Casebia was considered a VIE and concluded that it is not the primary beneficiary of the VIE. As such, the Company did not consolidate Casebia's results into the consolidated financial statements. See Note 4 for further details.

Intangible Assets

The Company's intangible assets consist of acquired intellectual property rights and relate to the Company's interest in TRACR. Intangible assets are recorded at fair value at the date of the business combination and are stated in the consolidated balance sheets net of accumulated amortization and impairments, if applicable. The Company evaluates the remaining useful life of intangible assets subject to amortization on a periodic basis to determine whether events and circumstances would indicate impairment or warrant a revision to the remaining useful life. If the estimate of an intangible asset's remaining useful life is changed, the Company amortizes the remaining carrying value of the intangible asset prospectively over the revised remaining useful life.

Intangible assets related to the acquired intellectual property rights are amortized over their estimated useful lives using the straight-line method as the pattern of revenues cannot be reasonably estimated. Amortization related to the acquired intellectual property rights is recorded in general and administrative expense in the consolidated statements of operations and comprehensive loss.

Net Loss Per Share Attributable to Common Shareholders

Basic net income (loss) per share is calculated by dividing net income (loss) attributable to common shareholders by the weighted-average number of common shares outstanding during the period. Diluted net income per share is calculated by dividing the net income attributable to common shareholders by the weighted-average number of common equivalent shares outstanding for the period, including any dilutive effect from outstanding stock options and warrants using the treasury stock method.

The following table sets forth the outstanding potentially dilutive securities that have been excluded in the calculation of diluted net loss per share because to do so would be anti-dilutive (in common stock equivalent shares):

	As of December 31,		
	2017	**2016**	**2015**
Convertible preferred shares	—	—	18,837,024
Conversion of convertible loans	—	—	4,110,987
Dr. Emmanuelle Charpentier call option	—	—	328,017
Outstanding options	6,262,339	4,535,371	1,939,986
Unvested unissued restricted shares	157,515	89,367	142,794
Total	6,419,854	4,624,738	25,358,808

Subsequent Events

The Company considered the events or transactions occurring after the balance sheet date, but prior to the issuance of the consolidated financial statements, for potential recognition or disclosure in its consolidated financial statements. All significant subsequent events have been properly disclosed in the consolidated financial statements.

Recent Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606) ("ASU 2014-09"). Subsequently, the FASB also issued ASU 2015-14, Revenue from Contracts with Customers (Topic 606), which adjusted the effective date of ASU 2014-09; ASU No. 2016-08, Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations (Reporting Revenue Gross versus Net), which amends the principal-versus-agent implementation guidance and illustrations in ASU 2014-09; ASU No. 2016-10, Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing, which clarifies identifying performance obligation and licensing implementation guidance and illustrations in ASU 2014-09; and ASU No. 2016-12, Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients, which addresses implementation issues and is intended to reduce the cost and complexity of applying the new revenue standard in ASU 2014-09 (collectively, the "Revenue ASUs").

The Revenue ASUs noted above provide an accounting standard for a single comprehensive model for use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance. The accounting standard is effective for interim and annual periods beginning after December 15, 2017, with an option to early adopt for interim and annual periods beginning after December 15, 2016. The guidance permits two methods of adoption: retrospectively to each prior reporting period presented (the full retrospective method), or retrospectively with the cumulative effect of initially applying the guidance recognized at the date of initial application (the modified retrospective method). The Company currently anticipates adopting the new standard effective January 1, 2018 under the modified retrospective method.

The Company has been monitoring FASB activity related to the new standard, as well as working with various non-authoritative groups to conclude on specific interpretative issues. The Company has established an implementation team to assess the impact of the standard on revenue recognition by reviewing our current accounting policies and practices to identify potential differences resulting from the application of the requirements of the new standard.

The Company has identified and are in the process of implementing appropriate changes to our business controls, processes, and systems to support recognition and disclosure under the Revenue ASUs. In addition, the Company continues to monitor additional changes, modifications, clarifications or interpretations undertaken by the FASB, which may impact its conclusions.

While the Company is substantially through our assessment of the new standard, the Company is still in the process of finalizing our implementation and determining the cumulative impact. The Company expects that under the new standard, the Company will continue to recognize revenue allocated to material rights to acquire certain licenses at a point in time when our collaboration partners exercise applicable options, which is consistent with our current revenue recognition model. The Company expects variable consideration from payments to R&D services will be allocable specifically to R&D services and will be recognized as earned under the new standard, whereas currently a portion of these payments are allocated to other undelivered elements, which could have a material impact on our financial statements. The impact will be recognized with a cumulative effect adjustment to equity at the date of initial application. The Company will adopt ASU 2014-09 effective January 1, 2018 using the modified retrospective transition method.

In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements—Going Concern* (Subtopic 205-40): Disclosure of Uncertainties about an Entity's ability to Continue as a Going Concern ("ASU 2014-15"), which requires management to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. This guidance is effective for the annual reporting period ending after December 15, 2016 and for annual and interim periods thereafter. The Company adopted ASU 2014-15 on December 31, 2016 and the adoption of ASU 2014-15 did not have an effect on our consolidated financial statements or disclosures.

In February 2016, the FASB issued ASU No. 2016-02, *Leases* ("ASU 2016-02"), which applies to all leases and will require lessees to record most leases on the balance sheet but recognize expense in a manner similar to the current standard. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018 and interim periods within those years, which is the year ended December 31, 2019 for the Company. Entities are required to use a modified retrospective approach of adoption for leases that exist or are entered into after the beginning of the earliest comparative period in the financial statements, with certain practical expedients available. The Company is evaluating the new guidance and the expected effect on its consolidated financial statements.

In March 2016, the FASB issued ASU No. 2016-09, Compensation—Stock Compensation (Topic 718) ("ASU 2016-09"). The guidance changes how companies account for certain aspects of equity-based payments to employees. Entities will be required to recognize income tax effects of awards in the income statement when the awards vest or are settled. The guidance also allows an employer to repurchase more of an employee's shares than it can under current guidance for tax withholding purposes providing for withholding at the employee's maximum rate as opposed to the minimum rate without triggering liability accounting and to make a policy election to account for forfeitures as they occur. The Company adopted the new standard January 1, 2017. The Company made an accounting policy election to account for the impact of pre-vesting forfeitures as they occur rather than applying an estimated forfeiture rate, as previously required. Adoption did not materially impact the consolidated financial statements.

In October 2016, the FASB issued ASU No. 2016-16, *Income Taxes* (Topic 740): *Intra-Entity Transfers of Assets Other Than Inventory* ("ASU 2016-16"), to improve the accounting for the income tax consequences of intra-entity transfers of assets other than inventory. Current guidance prohibits the recognition of current and deferred income taxes for an intra-entity asset transfer until the asset has been sold to an outside party, which is an exception to the principle of comprehensive recognition of current and deferred income taxes. The amendments in this update eliminate the exception for an intra-entity transfer of an asset other than inventory. The amendments should be applied on a modified retrospective transition basis, and are effective for fiscal years beginning after December 15, 2017, including interim periods within those fiscal years, and early adoption is permitted. The Company does not expect the adoption to have an impact on its financial statements.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash* ("ASU 2016-08"). ASU 2016-18 requires that a statement of cash flows explain the change during the period in the total cash, cash equivalents, and amounts generally described as restricted cash or restricted cash equivalents. Therefore, amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning and ending balances shown on the statement of cash flows. The guidance is effective beginning after December 15, 2017 and early adoption is permitted. ASU 2016-18 must be applied retrospectively to all periods presented. Upon adoption on January 1, 2018, the Company's 2017 and 2016 statement of cash flows will reflect an increase in operating cash flows resulting from the adoption of this new standard. The Company does not expect the adoption to have any additional impact on its financial statements.

In January 2017, the FASB issued ASU No. 2017-01, *Business Combinations* (Topic 805) ("ASU 2017-01"). ASU 2017-01 clarifies whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The purpose of the guidance is to narrow the definition of a business at it relates recording transactions as business acquisitions or asset acquisitions. The guidance is effective in annual periods beginning after December 15, 2017, including interim periods within those years, with early adoption permitted under certain circumstances. The Company does not expect the adoption to have an impact on its financial statements.

In May 2017, the FASB issued ASU 2017-09, Compensation – Stock Compensation ("Topic 718"): Scope Modification Accounting. The new standard is intended to reduce the diversity in practice and cost and complexity when applying the guidance in Topic 718 to a change to the terms or conditions of a share-based payment award. The new standard will be effective beginning January 1, 2019. The adoption of this standard is not expected to have a material impact on the Company's financial position or results of operations upon adoption.

3. Property and Equipment, net

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

	As of December 31, 2017	As of December 31, 2016
Computer equipment	$ 285	$ 110
Furniture, fixtures, and other	2,104	2,044
Laboratory equipment	6,603	2,970
Leasehold improvements	13,776	15,780
Construction work in process	—	1,065
	22,768	21,969
Accumulated Depreciation	(3,911)	(942)
Property and equipment, net	$ 18,857	$ 21,027

Depreciation expense for the year ended December 31, 2017, 2016, and 2015 was $3.0 million, $0.9 million, and $0.1 million, respectively.

4. Variable Interest Entities

TRACR Hematology Limited

On January 23, 2014, the founders of the Company formed TRACR in the United Kingdom, to further the development of the CRISPR/Cas9 technology into medicines for the treatment of blood-borne illnesses. On April 14, 2014, TRACR licensed certain foundational intellectual property rights under joint ownership from Dr. Emmanuelle Charpentier to develop and commercialize products for the treatment or prevention of human diseases related to hemoglobinopathies. See Note 9 for further details of the technology license agreement with Dr. Charpentier.

On April 14, 2014 the Company determined that it became the primary beneficiary of TRACR based on, among other factors, the Company's power to direct the activities that significantly impacted the economic performance of TRACR and the Company's financing of contractual obligations on behalf of TRACR, and the period in which the Company began to benefit from research and development of TRACR technology. Accordingly, the Company consolidated TRACR's financial statements as a consolidated VIE beginning on April 14, 2014.

On March 24, 2015, the Company acquired 4,600 ordinary shares of TRACR, representing 82.1% of the ordinary share capital, pursuant to a share exchange transaction with the shareholders of TRACR. Pursuant to the share exchange transaction on March 24, 2015, the Company also entered into a freestanding call option agreement with Dr. Charpentier for 1,000 ordinary shares of TRACR, representing the remaining 17.9% of the ordinary share capital of TRACR. Under the terms of the call option agreement, the Company has the option to acquire the remaining 1,000 shares of TRACR held by Dr. Charpentier in exchange for 328,017 Common Shares of the Company. Upon IPO in October 2016, the call option was exercised and the remaining non-controlling interest of TRACR was acquired, resulting in a reduction of Noncontrolling interest of $0.1 million, stock-based compensation of $0.2 million for original value of the call option, and additional paid-in capital of $0.1 million and TRACR became a wholly-owned subsidiary of the Company.

Joint Venture with Bayer Healthcare LLC

In December 2015, the Company entered into an agreement with Bayer to create a joint venture to discover, develop and commercialize new therapeutics for genetically linked diseases, including blood disorders, blindness and heart disease. On February 12, 2016, Casebia, a limited liability partnership, was formed in the United Kingdom. In March 2016 upon consummation of the JV, Bayer and the Company each received a 50% equity interest in the entity in exchange for their contributions to the entity. The Company determined that Casebia was considered a VIE and concluded that it is not the primary beneficiary of the VIE. As such, the Company did not consolidate Casebia's results into the consolidated financial statements. See Note 9 for further details.

5. Intangible Assets

The Company's intangible assets consist of acquired intellectual property rights related to the Company's initial consolidation of TRACR in April 2014. Acquired intellectual property rights had an estimated life of 10 years. Intangible assets, net of accumulated amortization, are as follows (in thousands):

Acquired intangible asset	Cost	Accumulated Amortization	Net
As of December 31, 2017	$ 547	$ (203)	$ 344
As of December 31, 2016	$ 547	$ (148)	$ 399

The Company recorded amortization expense of $0.1 million, $0.1 million, and $0.1 million for each of the years ended December 31, 2017, 2016, and 2015, respectively. As of December 31, 2017 and 2016, the remaining amortization period was 6.3 years and 7.3 years, respectively. The Company has not recorded any impairment charges for the years ended December 31, 2017, 2016 and 2015. The estimated future amortization of acquired intangible assets as of December 31, 2017 is expected to be as follows (in thousands):

For the Year Ended December 31,	Amount
2018	$ 55
2019	55
2020	55
2021	55
2022	55
Thereafter	69
Total amortization	$ 344

6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	As of December 31, 2017	2016
Payroll and employee-related costs	$ 5,550	$ 2,585
Research costs	2,285	996
Licensing fees	609	492
Professional fees	2,176	2,715
Intellectual property costs	500	3,372
Accrued property and equipment	—	5,081
Other	241	1,079
Total	$ 11,361	$ 16,320

7. Convertible Loans

2015 Convertible Loan Agreement with Vertex and certain existing shareholders

On October 26, 2015, the Company entered into a convertible loan agreement with Vertex and certain existing shareholders (the “Vertex Convertible Loan”) under which the Company could borrow up to $40.0 million. The Vertex Convertible Loan accrues interest at 2.5% per annum and had an initial maturity date of April 26, 2016 subject to acceleration upon the occurrence of certain conditions stated in the loan agreement (the “Maturity Date”). On various dates between November 23 and December 7, 2015, the Company borrowed aggregate net proceeds of $38.2 million. The Vertex Convertible Loan included various embedded conversion, redemption and other features, as further described below, none of which required separate accounting from the host instrument under ASC 815. On January 29, 2016, all of the outstanding principal plus accrued interest of $0.2 million under the Vertex Convertible Loan was automatically converted into 2,859,278 Series B Preferred Shares in connection with a qualified financing described below.

An event of default (“Event of Default”) is defined in the Vertex Convertible Loan Agreement and includes events of bankruptcy, insolvency or reorganization and, solely at the election of Vertex, a material breach that is not cured within the applicable notice and cure periods of the strategic collaboration, option and license agreement entered into by Vertex and the Company. See Note 9 for further details of the strategic, option and license agreement.

Conversion Terms

On the Maturity Date, the outstanding principal plus accrued interest automatically converts into Series B Preferred Shares at $9.33 per share.

In the event the Company issues equity securities prior to the Maturity Date with aggregate proceeds of not less than $50.0 million, of which $5.0 million is raised from investors other than Vertex or existing shareholders, the outstanding principal plus accrued interest under the Vertex Convertible Loan automatically converts into the newly issued equity securities at the price per share paid by the investors in the financing.

In the event of an underwritten public offering with shares of the Company listed on the New York Stock Exchange, the Nasdaq Global Market, or the Nasdaq Global Market, resulting in at least $50.0 million of proceeds to the Company closed prior to Maturity, the holders may elect, prior to the closing of the IPO, to convert the outstanding principal plus accrued interest into Series B Preferred Shares at $9.33 per share. Any Vertex Convertible Loan not converted prior to the closing of the IPO, shall automatically convert into Common Shares at a price paid by the investors for such shares in the IPO.

Upon a liquidation event prior to the Maturity Date, the holders may elect to convert the outstanding principal plus accrued interest into either Common Shares at a price of $9.33 per share or Series B Preferred Shares at a price of $9.33 per share.

Redemption Terms

Upon an Event of Default, all outstanding principal plus accrued interest becomes immediately due and payable.

Upon a liquidation event, if the holders do not exercise their conversion right, the outstanding principal plus accrued interest shall become due and payable in cash on the business day following the date on which the Company or its shareholders receive the proceeds from the liquidation event.

Contingent Interest

Upon an Event of Default, the outstanding amount of the Vertex Convertible Loan shall bear, in addition to the base interest of 2.5% per annum, default interest at a rate of 7.5% per annum.

Convertible Loan with Bayer HealthCare LLC

Concurrent with the execution of the Bayer Joint Venture agreement, the Company also entered into a Convertible Loan Agreement (“Bayer Convertible Loan”) with Bayer for $35.0 million. The Bayer Convertible Loan accrued interest at 2.0% per annum and matured on January 29, 2016 (the “Maturity Date”). On January 29, 2016, the Company issued the Bayer Convertible Loan in exchange for aggregate net proceeds of $35.0 million. The Bayer Convertible Loan included various embedded conversion, redemption and other features, none of which required separate accounting from the host instrument under ASC 815.

Conversion of Convertible Loans to Series B Preferred Shares

On January 29, 2016, concurrent with the issuance of the Bayer Convertible Loan, all of the outstanding principal under the $35.0 million Bayer Convertible Loan automatically converted into 2,605,330 Series B Preferred Shares at $13.43 per share. The Company determined the fair value of the Bayer Convertible Loan to be $24.5 million based on the fair value of the underlying Series B Preferred Shares that were exchanged as part of the immediate conversion. As the Bayer Convertible Loan was executed in contemplation of the joint venture agreement with Bayer, the Company evaluated the Bayer Convertible Loan as part of one multiple-element arrangement and using a relative fair value allocation allocated $27.0 million of aggregate arrangement consideration to the Bayer Convertible Loan upon issuance (See Note 9). Upon conversion, the Company accreted the Bayer Convertible Loan to its face value of $35.0 million through a charge to interest expense of $8.0 million and converted the $35.0 million to Series B Preferred Shares under the conversion model.

The receipt of $35.0 million in proceeds under the Bayer Convertible Loan in exchange for equity securities, combined with the $38.2 million in proceeds from Vertex Convertible Loan, represented a qualified financing, as defined, and triggered an automatic conversion provision of the Vertex Convertible Loan Agreement. Accordingly, on January 29, 2016, the Vertex Convertible Loan, including loans from existing shareholders, plus accrued interest also converted into 2,859,278 of Series B Preferred Shares at $13.43 per share. The Company determined the fair value of the Vertex Convertible Loan to be $26.9 million based on the fair value of the underlying Series B Preferred Shares that were exchanged as part of the conversion. Upon extinguishment, the Company recorded a gain on extinguishment of $11.5 million for the difference between the carrying value of the debt and the fair value of the Series B Preferred Shares issued to settle the debt under the general extinguishment model.

8. Commitments and Contingencies

Operating Leases

As of December 31, 2017, the Company had operating leases for office, laboratory, and corporate housing spaces. The lease of the Company’s research facility space expires in February 2022, with one optional five-year extension period. The sublease of the Company’s primary office and research facility space expires in December 2026. Rental expense for the years ended December 31, 2017, 2016, and 2015 was $6.9 million, $4.2 million, and $1.3 million, respectively. The Company expenses rent, including tenant improvement allowances received by the Company, on a straight-line basis over the term of the lease, including any rent-free periods.

In May 2016, the Company entered into a sublease pursuant to which it subleases in Cambridge, Massachusetts (the “610 Main Street Sublease”) the Company’s primary research and US office facility. The initial term of the 610 Main Street will expire on December 22, 2026. The Company has an option to extend the term of the 610 Main Street Sublease for an additional five year period if, at the time of expiration of the initial term, the sublessor does not intend to utilize the space for itself or its affiliates. The 610 Main Street Sublease contains escalating rent clauses which require higher rent payments in future years.

In March 2017, the Company entered into an agreement pursuant to which it has the right to use certain office facilities in Zug, Switzerland. The original term expires in September 2017 with an automatic renewal for a six-month term. The Company’s obligations under this right to use agreement are secured by a cash deposit in the approximate amount of CHF 11 thousand held by the office space provider.

Future minimum payments required under the leases as of December 31, 2017, are as follows (in thousands):

Years Ended December 31,	Amount
2018	$ 4,908
2019	6,369
2020	6,823
2021	7,027
2022	5,875
Thereafter	24,494
Total minimum lease payments	$ 55,496

The amounts above are net of payments to be received under a sublease agreement, totaling $1.5 million in 2018 and $0.3 million in 2019.

Letters of Credit

As of December 31, 2017 and 2016, the Company had restricted cash of $3.2 million and $3.2 million, respectively, representing letters of credit securing the Company's obligations under certain leased facilities in Cambridge, Massachusetts at 200 Sidney Street and the 610 Main Street as well as certain credit card arrangements. The letters of credit are secured by cash held in a restricted depository account. The cash deposit is recorded in restricted cash in the accompanying consolidated balance sheet as of December 31, 2017 and 2016.

Shareholder Settlement

Under the terms of a shareholder agreement existing prior to the IPO in 2016, if a U.S. common shareholder elected to file a Qualified Electing Fund ("QEF") and notified the Company of this election, the Company was required to make advance payments to the shareholder related to their individual tax liability. In September 2016, the Company formally offered an aggregate settlement of up to $2.0 million to certain U.S common shareholders in order to release the Company from any and all obligations or claims concerning and/or arising out of the Company's status as a PFIC or a Controlled Foreign Corporation (a "CFC") for any taxable year from 2013 through 2015, including for potential lack of timely notification of the Company's PFIC status (an "Annual Information Statement") for the year ended December 31, 2015.

Following the formal settlement offer in September 2016, in the fourth quarter of 2016 the Company made payments to shareholders of $2.0 million, respectively, under the terms of the accepted settlements. The obligation to make advance payments under the shareholder agreement for tax years subsequent to 2015 terminated upon the closing of the IPO.

The Company has made available a 2017 and 2016 PFIC Annual Information Statement on its website for its shareholders.

Research Agreements

The Company has engaged several research institutions and companies to identify new delivery strategies and applications of the CRISPR/Cas9 technology. As a result of these efforts, the Company sponsored research programs during 2017. In association with these agreements, the Company has committed to making payments for related research and development services of $0.3 million, and $0.1 million in 2018 and 2019, respectively.

The Company is also a party to a number of research license agreements which require upfront payments, future royalty payments and potential milestone payments from time to time which could be significant. In association with these agreements, the Company has committed to making payments for related research and development services of $0.5 million, and $0.4 million in 2018 and 2019, respectively. In connection with these agreements, the Company has made upfront payments of $4.4 million and milestone payments of $1.4 million through December 31, 2017.

Litigation

The Company licenses a U.S. patent application that is currently subject to interference proceedings declared by the Patent Trial and Appeal Board ("PTAB") of the U.S. Patent and Trademark Office. Following motions by the parties and other procedural matters, the PTAB concluded in February 2017 that the declared interference should be dismissed because the claim sets of the two parties were not directed to the same patentable invention in accordance with the PTAB's two-way test for patent interferences. In April

2017, the regents of the University of California (“California”) appealed the PTAB decision to the U.S. Court of Appeals for the Federal Circuit. In the appeal, California is seeking review and reversal of the PTAB’s February 2017 decision, which terminated the interference without determining which inventors actually invented the use of the CRISPR/Cas9 genome editing technology in eukaryotic cells.

9. Significant Contracts

Intellectual Property Agreements

CRISPR Therapeutics AG—Charpentier License Agreement

In April 2014, the Company entered into a technology license agreement with Dr. Emmanuelle Charpentier pursuant to which the Company licensed certain intellectual property rights under joint ownership from Dr. Charpentier to develop and commercialize products for the treatment or prevention of human diseases other than hemoglobinopathies (“CRISPR—Charpentier License Agreement”). In consideration for the granting of the license, the Company paid Dr. Charpentier an upfront fee of CHF 0.1 million ($0.1 million) and agreed to pay an immaterial annual license maintenance fee if Dr. Charpentier is not otherwise engaged in a service arrangement with the Company. During the years ended December 31, 2017, 2016 and 2015, Dr. Charpentier has been in a consulting arrangement with the Company, as such, no annual payments have been made under this provision. Dr. Charpentier is entitled to receive nominal clinical milestone payments. The Company is also obligated to pay Dr. Charpentier a low single digit percentage of sublicensing payments received under any sublicense agreement with a third party. In addition, the Company is also obligated to pay to Dr. Charpentier a low single-digit percentage royalty based on annual net sales of licensed products and licensed services by the Company and its affiliates and sublicensees.

During the years ended December 31, 2017, 2016, and 2015 the Company recorded and accrued $0 million, $0.5 million, and $0.9 million, respectively, of sublicensing fees due to Dr. Emmanuelle Charpentier in research and development expense under the terms of the CRISPR—Charpentier License Agreement that was triggered by the execution of the Vertex collaboration agreement and the Bayer agreement.

TRACR Hematology Limited—Charpentier License Agreement

In April 2014, TRACR entered into a technology license agreement (“TRACR—Charpentier License Agreement”) with Dr. Emmanuelle Charpentier pursuant to which TRACR licensed certain intellectual property rights under joint ownership from Dr. Charpentier to develop and commercialize products for the treatment or prevention of human diseases related to hemoglobinopathies. In consideration for the granting of the license, Dr. Charpentier is entitled to receive nominal clinical milestone payments. TRACR is also obligated to pay Dr. Charpentier a low single digit percentage of sublicensing payments received under any sublicense agreement with a third party. In addition, TRACR is obligated to pay to Dr. Charpentier low single digit percentage royalties based on annual net sales of licensed products and licensed services by the Company and its affiliates and sublicensees.

During each of the years ended December 31, 2017, 2016, and 2015 the Company recorded an immaterial amount of sublicensing fees due to Dr. Emmanuelle Charpentier in research and development expense under the terms of the TRACR—Charpentier License Agreement that was triggered by the execution of the Vertex collaboration agreements.

Invention Management Agreement

On December 15, 2016, the Company entered into an IMA, with the University of California (“California”), the University of Vienna (“Vienna”), Dr. Charpentier, Intellia therapeutics, Inc. (“Intellia”), Caribou Biosciences, Inc. (“Caribou”), ERS Genomics Ltd., or (“ERS”), and TRACR. Under the IMA, California and Vienna retroactively consent to Dr. Charpentier’s licensing of her rights to the CRISPR/Cas9 intellectual property, pursuant to the license the Company has with Dr. Charpentier, to the Company, and wholly-owned subsidiary TRACR, and ERS, in the United States and globally. The IMA also provides retroactive consent of co-owners to sublicenses granted by us, TRACR and other licensees, prospective consent to sublicenses they may grant in future, retroactive approval of prior assignments by certain parties, and provides for, among other things, (i) good faith cooperation among the parties regarding patent maintenance, defense and prosecution, (ii) cost-sharing arrangements, and (iii) notice of and coordination in the event of third-party infringement of the subject patents and with respect to certain adverse claimants of the CRISPR/Cas9 intellectual property. Unless earlier terminated by the parties, the IMA will continue in effect until the later of the last expiration date of the patents underlying the CRISPR/Cas9 technology, or the date on which the last underlying patent application is abandoned. Under the IMA the Company is obligated to share costs related to patent maintenance, defense and prosecution. For the years ended December 31, 2017, 2016, and 2015 the Company incurred $1.2 million, $2.8 million and $1.5 million respectively, in shared costs. The Company had accrued legal costs from the cost sharing of $0.4 million and $2.8 million as of December 31, 2017 and December 31, 2016, respectively.

Patent Assignment Agreement

In November 2014, the Company entered into a patent assignment agreement ("Patent Assignment Agreement") with Dr. Emmanuelle Charpentier, Dr. Ines Fonfara, and Vienna (collectively, the "Assignors"), pursuant to which the Company was assigned all rights, title and interest in and to certain patent rights claimed in the U.S. Patent Application No.61/905,835. In consideration for the assignment of such rights, the Assignors are entitled to receive clinical milestone payments totaling up to €0.3 million (approximately $0.4 million) in the aggregate for the first human therapeutic product. The Company is also obligated to pay to the Assignors low single digit royalties based on annual net sales of licensed products and licensed services by the Company and its affiliates and sublicensees.

During the years ended December 31, 2017, 2016, and 2015 the Company recorded $0 million, $33 thousand, and $0.1 million, respectively, of sublicensing fees due to the Assignors in research and development expense under the terms of the Patent Assignment Agreement that was triggered by the execution of the Vertex collaboration agreement and the Bayer Agreement.

Collaboration Agreement and JDA with Vertex Pharmaceuticals, Incorporated

Summary of Agreement

On October 26, 2015, the Company entered into a strategic collaboration, option, and license agreement ("Collaboration Agreement") with Vertex, focused on the use of CRISPR's gene editing technology, known as CRISPR/Cas9, to discover and develop potential new treatments aimed at the underlying genetic causes of human disease. On December 12, 2017, the Company and Vertex entered into Amendment No. 1 to the Collaboration Agreement, or the (the " Amendment"). The Amendment, among other things, modified certain definitions and provisions of the Collaboration Agreement to make them consistent with the JDA and clarified how many options are exercised (or deemed exercised) in connection with certain targets specified under the Collaboration Agreement. The Amendment also amended other provisions of the Collaboration Agreement, including the expiration terms of the Collaboration Agreement.

Summary of Collaboration Agreement

The collaboration will evaluate the use of CRISPR-Cas9 across multiple diseases where targets have been validated through human genetics. Vertex and CRISPR will focus their initial gene editing research on discovering treatments to address the mutations and genes known to cause and contribute to sickle cell disease ("SCD"), beta-thalassemia and cystic fibrosis. Vertex and CRISPR will also evaluate a specified number of other genetic targets as part of the collaboration. For up to six targets, Vertex has an exclusive option to obtain: (1) an exclusive license to commercialize CRISPR technology or (2) a co-exclusive license with respect to hemoglobinopathy and beta-globin targets.

The collaborative program of research to be undertaken by the parties pursuant to the Collaboration Agreement will be conducted in accordance with a mutually agreed upon research plan which outlines each party's research and development responsibilities across the three research areas. The Company's research and development responsibilities under the research plan ("R&D Services") are related to generating genome editing reagents that modify gene targets selected by Vertex. Except with respect to the Company's obligations under the mutually agreed upon research plan, Vertex has sole responsibility, at its own costs, for the worldwide research, development, manufacturing and commercialization of products resulting from the exclusive licenses obtained.

The research collaboration will end on the earlier of the date on which Vertex has exercised six options to obtain exclusive/co-exclusive licenses with respect to a collaboration target, or the fourth anniversary of the effective date of the agreement. The research term may be extended as mutually agreed by the parties up to nine additional months to complete any research activities under the approved research plan that are incomplete on the fourth anniversary of the effective date.

The Collaboration Agreement will be managed on an overall basis by a project leader from each of the Company and Vertex. In addition, the activities under the collaboration agreement during the research term will be governed by a joint research committee ("JRC") formed by an equal number of representatives from the Company and Vertex. Decisions by the JRC will be made by consensus of the group, however, Vertex will have final decision-making authority in the event of disagreement, provided it is in good faith and not contrary to any explicit clause of the agreement.

In connection with the Collaboration Agreement, Vertex made a nonrefundable upfront payment of $75.0 million. In addition, Vertex will fund all of the discovery activities conducted pursuant to the agreement. For potential hemoglobinopathy treatments, including treatments for sickle cell disease, the Company and Vertex will share equally all research and development costs and worldwide revenues. For other targets that Vertex elects to license, Vertex would lead all development and global commercialization activities. For each of up to six targets that Vertex elects to license, other than hemoglobinopathy and beta-globin targets, the Company has the potential to receive up to $420.0 million in development, regulatory and commercial milestones and royalties on net product sale.

Vertex is entitled to terminate the Collaboration Agreement as a whole, or terminate the Collaboration Agreement in part with respect to a particular collaboration program, for convenience by providing the Company 90 days' written notice of such termination; provided, however, that if any termination applies to a product for which Vertex has received marketing approval, Vertex will provide CRISPR no less than 270 days' notice of such termination. If Vertex is in material breach of this Collaboration Agreement, the Company has the right to terminate the Collaboration Agreement in full at its discretion 90 days after delivery of written notice to Vertex.

Summary of Amendment and JDA

Under the terms of the Collaboration Agreement, Vertex was given a total of six target options available to be exercised. Upon execution of the JDA and Amendment, Vertex exercised two of its original six options to develop and commercialize hemoglobinopathy and beta-globin targets. Under the terms of the JDA and Amendment, inclusion of further hemoglobinopathy targets will require mutual agreement of the Parties and will not require Vertex to exercise additional options.

In connection with entering into the JDA, the Company received a $7.0 million up-front payment from Vertex and is eligible for a one-time low seven-digit milestone payment upon the dosing of the second patient in a clinical trial with the initial product candidate. The net profits and net losses, as applicable, incurred under the JDA will be shared equally between us and Vertex.

CRISPR and Vertex will form the following committees: (i) a joint steering committee to provide high-level oversight and decision making regarding the activities covered by the JDA, (ii) a joint development committee to provide oversight and decision making-making regarding development activities, (iii) a joint commercialization committee to provide oversight and decision-making regarding commercialization activities and (iv) a joint manufacturing committee to provide oversight and decision-making regarding manufacturing activities. Each of the committees will contain an equal number of representatives from each of CRISPR and Vertex.

The JDA provides that the Company will be responsible for commercialization activities in the United States and Vertex will be responsible for commercialization activities outside of the United States.

Either party can terminate the JDA upon the other party's material breach, subject to specified notice and cure provisions, or, in the case of Vertex, in the event that the Company becomes subject to specified bankruptcy, winding up or similar circumstances. Either party may terminate the JDA in the event the other party commences or participates in any action or proceeding challenging the validity or enforceability of any patent that is licensed to such challenging party pursuant to the JDA. Vertex also has the right to terminate the JDA for convenience at any time after giving prior written notice.

If circumstances arise pursuant to which a party would have the right to terminate the JDA on account of an uncured material breach, such party may elect to keep the JDA in effect and cause such breaching party to be treated as if it had exercised its opt-out rights with respect to the products associated with such uncured material breach (described below) and the royalties payable to the breaching party would be reduced by a specified percentage.

Either party may opt of out of the development of a product candidate under the JDA after predetermined points in the development of the product candidate, on a candidate-by-candidate basis. In the event of such opt-out, the opting-out party will no longer share in the net profits and net losses associated with such product candidate and, instead, the opting out party will be entitled to high single to mid- teen percentage royalties on the net sales of such product, if commercialized. Vertex shall have no obligation to pay the Company any milestone payments with respective to an opt-out product.

Accounting for the Collaboration Agreement, Amendment and JDA

The Company determined that the Amendment and JDA represented a modification to the original Collaboration Agreement. As a result, the Company evaluated all remaining units of account within the modified contract and allocate to those units (based on their relative selling prices) the sum of (1) additional consideration related to the Amendment and JDA and (2) any deferred revenue from the Collaboration Agreement using current estimated prices for each of the units.

The arrangement includes components of a customer-vendor relationship and a collaborative arrangement as defined under ASC 808. The Company will apply the guidance of ASC 605-25 by analogy to the units of account of the Collaboration Agreement and the units of account of the JDA subject to ASC 605-25 as outlined below. The Company will apply the guidance of ASC 808 to the on-going collaborative and development components of the JDA including the (i) development and commercialization services for currently identified shared products; (ii) R&D services for any follow-on products subject to the JDA; and (iii) committee participation.

The Company evaluated the Collaboration Agreement, Amendment and JDA in accordance with the provisions of ASC 605-25. The Company's arrangement with Vertex contains the following deliverables: (i) a non-exclusive research license; (ii) an option to obtain an exclusive license for up to four Collaboration Targets; (iii) co-exclusive development and commercialization licenses for hemoglobinopathy and beta-globin targets identified in the JDA; (iv) co-exclusive research license for the follow-on products; (v) the performance of R&D Services under the Collaboration Agreement; and (vi) JRC participation under the Collaboration Agreement.

Management considered whether any of these deliverables could be considered separate units of accounting. Regarding the non-exclusive research license, the Company concluded that it does not have stand-alone value separate from the options to exercise the exclusive or the exercised co-exclusive licenses since Vertex would not benefit from acquiring a research license without the ability to obtain the license to commercialize the results of that research. As a result, the Company concluded that the research license should be combined with those options. Regarding the co-exclusive research license for the follow-on products, the Company concluded that it does not have stand-alone value separate from the exercised co-exclusive licenses under the JDCA since Vertex would not benefit from acquiring a research license without the license to commercialize the results of that research. The Company concluded the co-exclusive research license should be combined separately with each development and commercialization co-exclusive license granted under the JDA.

Regarding the R&D Services under the Collaboration Agreement, the Company concluded that there are other vendors in the market that could perform the related services. As such the Company concluded the R&D Services represent a separate unit of accounting.

Regarding the JRC obligations, the Company concluded that the JRC obligations deliverable has standalone value from the option to license because the services could be performed by an outside party. As such the Company concluded the JRC obligations represent a separate unit of accounting.

As a result, management concluded that there following the modification are four units of accounting: (i) four individual combined units of accounting representing the non-exclusive research license, and the option for up to four exclusive licenses to develop and commercialize the collaboration targets; (ii) four individual combined units of accounting representing the co-exclusive research license, and a development and commercialization license to develop and commercialize hemoglobinopathies and beta-globin targets; (iii) the performance of R&D Services; and (iv) the participation in the JRC.

The Company has determined that neither VSOE of selling price nor TPE of selling price is available for any of the units of accounting identified. Accordingly, the selling price of each unit of accounting was determined based on the Company's BESP. The Company developed the BESP for all of the units of accounting included in the Collaboration Agreement and JDA with the objective of determining the price at which it would sell such an item if it were to be sold regularly on a standalone basis.

The Company developed the BESP for the R&D Services and the JRC participation primarily based on the nature of the services to be performed and estimates of the associated effort and cost of the services, adjusted for a reasonable profit margin that would be expected to be realized under similar contracts. The Company's BESP for the remaining R&D Services was $4.0 million. The Company's BESP for the JRC participation services was de minimis based on an estimate of time spent on preparation, participation, review and travel for the meetings.

The Company's BESP for the remaining four combined units of the non-exclusive research license and the options for an exclusive license to develop and commercialize a single collaboration target are $55.6 million, $48.4 million, $27.3 million and $27.3 million for a total of $158.6 million. BESPs for these items were determined based on probability and present value adjusted cash flows from the milestones payments owed for exclusive licenses outlined in the Collaboration Agreement. BESP reflects the level of risk and expected probability of success inherent in the nature of the associated research area.

The Company's BESP for the co-exclusive research license and the development and commercialization licenses for of the hemoglobinopathy and beta-globin targets is $48.9 million. BESP for this item was determined based on probability and present value adjusted cash flows from the equal sharing of project worldwide net profit or net loss. BESP reflects the level of risk and expected probability of success inherent in the nature of the associated research area.

Allocable arrangement consideration is comprised of: (i) deferred revenue of $80.0 million; (ii) an upfront payment of $7.0 million under the JDA; (iii) the estimated R&D services of $4.0 million; and (iv) payments related to the estimated exercise of options on future exclusive licenses for four targets of $40.0 million. The aggregate allocable arrangement consideration of $131.0 million was allocated among the separate units of accounting using the relative selling price method as follows: (i) four individual combined units of accounting representing the non-exclusive research license, and the option for up to four exclusive licenses to develop and commercialize the collaboration targets: $34.4 million, $30.0 million, $16.9 million and $16.9 million for a total of $98.2 million; (ii) four individual combined units of accounting representing the co-exclusive research license, and a development and commercialization license to develop and commercialize each of the hemoglobinopathy and beta-globin targets: $30.3 million; and (iii) the performance of R&D Services: $2.5 million.

Regarding each of the four individual combined units of accounting representing the non-exclusive research license, and the option for up to four exclusive licenses to develop and commercialize the collaboration targets, the Company will defer recognition of the amount attributable to each unit of accounting until the respective option is exercise. If Vertex ultimately fails to exercise any of the remaining license options, any remaining amount allocated to the combined unit of account would be recognized when the Company's applicable option expires, provided that revenue recognized will be limited to cash received under the arrangement.

Upon the execution of the JDA, a research, development and commercialization license has been granted for hemoglobinopathy and beta-globin targets. The Company determined that these licenses were delivered at inception of the JDA and $30.3 million in revenue was recognized for this unit of accounting in December 2017.

Consistent with the Company's original accounting policy, the amounts allocated to R&D Services will be recognized as the R&D Services are performed.

Milestones under the Collaboration Agreement

The Company has evaluated all of the milestones that may be received in connection with the Collaboration Agreement. In evaluating if a milestone is substantive, the Company assesses whether: (i) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the Company's performance to achieve the milestone, (ii) the consideration relates solely to past performance, and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company notes that the $10.0 million due upon the exercise of each option for an Exclusive License was determined to be part of the fixed and determinable consideration allocable at contract inception and is not subject to milestone method accounting.

The first potential milestone the Company will be entitled to receive is the milestone in the JDA to receive a one-time low seven-digit milestone payment in any clinical trial in the initial shared product. The Company determined that this payment represents the definition of a milestone under ASC 605-28 as: 1) dosing a patient in the initial shared product can only be achieved partially through CRISPR's performance as they are co-developing the product, 2) while it is likely that this event will occur, there is uncertainty that the event will be achieved given the nature of clinical development and the stage of the CRISPR technology and 3) achievement of this milestone will result in an additional low seven- digit milestone payment being due to the Company. Additionally, the $10.0 million milestone due upon the filing of an Investigational New Drug Application ("IND") for a selected Exclusive License under the Collaboration Agreement. As the developmental milestone of the agreement relates to the filing of an IND, the Company has considered it to be substantive. Accordingly, such amounts will be recognized as revenue in full in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. There are no other substantive milestones.

As such the total amount of substantive milestones subject to milestone method accounting treatment is $10.0 million for each selected Exclusive License and a one-time low seven-digit milestone payment for the JDA upon dosing of the second patient in any clinical trial in the initial shared product.

The remaining milestones are predominately related to the development and commercialization of a product resulting from the arrangement and are payable with respect to each selected Exclusive License. Each milestone is payable only once per collaboration target, regardless of the number of products directed to such collaboration target that achieve the relevant milestone event. There are nine remaining clinical development and regulatory approval milestones which may trigger proceeds of up to $90.0 million and $235.0 million, respectively, for each selected Exclusive License, and two commercial milestones which may trigger proceeds of up to $75.0 million for each selected Exclusive License (which, when combined with the $10.0 million due upon exercise of the exclusive option and the $10.0 million development milestone associated with an IND, total $420.0 million for each selected Exclusive License), as follows:

Developmental Milestone Events

1. Initiation of the first Clinical Trial of a Product
2. Establishment of POC for a Product
3. Initiation of the first Phase 3 Clinical Trial of a Product
4. Acceptance of Approval Application by the FDA for a Product
5. Acceptance of Approval Application by the EMA for a Product
6. Acceptance of Approval Application by a Regulatory Authority in Japan for a Product
7. Marketing Approval in the US for a Product

8. Marketing Approval in the EU for a Product
9. Marketing Approval in Japan for a Product

Commercial Milestone Events

1. Annual Net Sales for Products with respect to a Collaboration Target exceed $500 million
2. Annual Net Sales for Products with respect to a Collaboration Target exceed $1.0 billion

After Vertex has exercised an Exclusive License option, Vertex will be solely responsible for all research, development, manufacturing, and commercialization of licensed agents and products for the relevant target. As the Company's involvement in this process is limited to observer status, management determined that milestones are not considered substantive because they do not relate solely to the past performance of the Company. Upon the achievement of a milestone, management will evaluate whether the triggering event occurs during or after the research term. If the triggering event occurs during the research term, management has elected to treat the milestone similar to an up-front payment. In these cases, if and when any of these milestones are received, the amount will be included in the overall arrangement consideration and allocated to the remaining identified deliverables. To the extent all deliverables have been satisfied, any additional consideration allocated to them could be immediately recognized. If the triggering event occurs after the research term, the Company will recognize the associated revenue in the period in which the event occurs. The Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

During the year ended December 31, 2017, 2016, and 2015, the Company recognized $36.2 million, $4.0 million, and $0.2 million of revenue with respect to the collaboration with Vertex. Research and development expense incurred by the Company in relation to its performance under the collaboration agreement for the years ended December 31, 2017 and 2016 was $9.9 million and $7.0 million, respectively. As of December 31, 2017 and 2016, there is $56.8 million and $77.1 million of non-current deferred revenue related to the Company's collaboration with Vertex, respectively.

Joint Venture with Bayer Healthcare LLC

On December 19, 2015, the Company entered into an agreement to establish a joint venture ("Bayer Joint Venture") to research the development of new therapeutics to cure blood disorders, blindness, and congenital heart disease. On February 12, 2016, the Company and Bayer completed the formation of the joint venture entity, Casebia, a limited liability partnership formed in the United Kingdom. Bayer and the Company each received a 50% equity interest in the entity in exchange for their contributions to the entity. The Company contributed $0.1 million in cash and licensed its proprietary CRISPR/Cas9 gene editing technology and intellectual property for selected disease indications. Bayer contributed its protein engineering expertise and relevant disease know-how.

Bayer will provide up to $300.0 million in research and development funding to Casebia over the first five years, subject to certain conditions, of which the first $45.0 million was contributed upon formation in the first quarter of 2016. Under the joint venture agreement, the Company has no obligation to provide any additional funding and the Company's ownership interest will not be diluted from future contributions from Bayer. The activities of Casebia are controlled by a management board under the joint control of the Company and Bayer. As Casebia is jointly controlled by the Company and Bayer, the Company accounts for its 50% interest using the equity method of accounting.

Under the agreement, Casebia will pay the Company up to $35.0 million in exchange for a worldwide, exclusive license to commercialize the Company's CRISPR/Cas9 technology specifically for the indications designated by Casebia. In March 2016, the Company received a non-refundable up-front payment of $20.0 million as a technology access fee. The remaining $15.0 million was paid on December 22, 2016 following delivery of the necessary consents from patent holders of the Company's intellectual property. There are no milestone, royalties or other payments due to the Company under this aspect of the agreement. The Company determined that the contribution of the CRISRP/Cas9 technology by license to Casebia did not meet the definition of a business under ASC 805.

The Company will also provide to Casebia compensated research and development services through a separate agreement.

Concurrent with the execution of the Bayer Joint Venture agreement, the Company also entered into the Bayer Convertible Loan for $35.0 million.

As the Bayer Joint Venture (including the CRISPR/Cas9 technology license and the research and development services) and the Bayer Convertible Loan were executed at the same time, the Company determined that they should be evaluated as one multiple-element arrangement. Additionally, the Company also determined that ASC 845, *Nonmonetary Transactions* ("ASC 845") did not apply to this arrangement given the Company's significant continuing involvement with Casebia and the amount of cash involved in the arrangement. As a result, the Company analogized to ASC 605-25 in allocating the relative fair value of the consideration received to the different elements of the arrangement.

The Company allocated the fair value of the consideration received using a relative fair value allocation. The allocable arrangement consideration included (i) the total cash payment by Casebia for the technology access fee, net of the Company's $0.1 million contribution, of $34.9 million, (ii) the fair value of the equity interest in the Joint Venture of $36.4 million, (iii) the $35.0 million received from the issuance of the Convertible Debt, and (iv) $6.3 million of estimated cash consideration to be received under the research and development service arrangement, accumulating to $112.6 million.

The Company identified the following elements under the transaction:

(i) Combined element of an exclusive, worldwide, royalty free, license to the CRISPR/Cas9 technology specifically for the indications designated by Casebia, and delivery of the consents of the assignors of the underlying patents to the technology to develop, manufacture, and commercialize licensed products under that license

(ii) Research and development services, and

(iii) The issuance of the Bayer Convertible Loan.

The Company determined the fair value of the license was $71.4 million based on the consideration paid and the fair value of the 50% interest in Casebia, which was determined utilizing discounted cash flows based on reasonable estimates and assumptions of cash flows expected from Casebia. The fair value of the separate research and development services was determined to be $6.3 million. The fair value of the Bayer Convertible Loan was determined to be $24.5 million, based on the fair value of the underlying preferred shares that were exchanged as part of the immediate conversion. Using a relative fair value allocation, the Company allocated the aggregate arrangement consideration paid as follows:

(i) $63.6 million was allocated to the license and patent holder consent combined element

(ii) $0.6 million was allocated to the future research and development services

(iii) $27.0 million was allocated to the Bayer Convertible Loan

The difference between combined above amounts of $91.2 million and the total allocable arrangement consideration of $112.6 million is due to allocable arrangement consideration associated with the $6.3 million of estimated cash consideration to be received under the research and development service arrangement and the remaining $15.0 million of the license fee paid upon the delivery of the consent from the patent holders of the Company's intellectual property.

Following delivery of the patent holders' consent, which occurred on December 17, 2016, the combined amount attributed to the license and patent holder consent element and the remaining $15.0 million license fee, which amount to $78.6 million, was recognized as other income for the year ended December 31, 2016. The Company had determined that the license and patent holder consent combined element did not meet the definition of revenue because the licensing of its technology in connection with the formation of a joint venture is not part of the Company's major ongoing or central operations.

As the amount allocated to the Bayer Convertible Loan represents an $8.0 million discount to its $35.0 million face value, the Company recognized interest expense during the twelve months ended December 31, 2017 equal to the discount. The Convertible Loan automatically converted into Series B preferred shares on its January 29, 2016 maturity date.

During 2016, the Company recorded an equity method investment of $36.5 million equal to the fair value of the Company's interest in Casebia (which was included in the allocable arrangement consideration described above). Following delivery of the patent holders consent element and realization of the described gain allocated to the license and patent holder consent combined element, the Company recorded unrealized equity method losses up to the remaining amount of the $36.5 million investment.

During the year ended December 31, 2017, the Company recognized $4.8 million, of revenue with respect to the collaboration with Casebia. Research and development expense incurred by the Company in relation to its performance under the agreement for the year ended December 31, 2017 was $4.5 million. As of December 31, 2017, there is $0.1 million of non-current deferred revenue related to the Company's collaboration with Casebia, respectively. Unrecognized equity method losses in excess of the Company's investment in Casebia totaled $21.2 million as of and for the year ended December 31, 2017. During 2017, the Company recorded $1.8 million of stock-based compensation expense related to Casebia employees.

During the year ended December 31, 2016, the Company recognized $1.2 million, of revenue with respect to the collaboration with Casebia. Research and development expense incurred by the Company in relation to its performance under the agreement for the year ended December 31, 2016 was $1.2 million. As of December 31, 2016, there is $0.5 million of non-current deferred revenue related to the Company's collaboration with Casebia, respectively. Unrecognized equity method losses in excess of the Company's investment in Casebia totaled $4.0 million as of and for the year ended December 31, 2016. During 2016, the Company recorded $0.2 million of stock-based compensation expense related to Casebia employees.

Total operating expenses, and net loss of Casebia for the twelve months ended December 31, 2017 was $36.3 million and $36.2 million, respectively. Total operating expenses, and net loss of Casebia for the twelve months ended December 31, 2016 was $80.8 million, which included research and development expenses equal to $77.4 million for the fair value of the CRISPR license acquired.

Subscription Agreement with Bayer Global Investments B.V.

On December 19, 2015, the Company entered into a subscription agreement, ("Subscription Agreement"), with Bayer BV. Pursuant to the Subscription Agreement, Bayer BV was given the option, at its election, to purchase $35.0 million of the Company's Common Shares in a private placement concurrent with the Company's IPO at a per share price equal to the public offering price.

10. Redeemable Convertible Preferred Shares

Upon the closing of the Company's IPO on October 24, 2016, all outstanding Preferred Shares of the Company were automatically converted into 27,135,884 Common Shares on a one-for-one basis. As of December 31, 2017 and 2016, the Company had no Preferred Stock authorized, issued, or outstanding.

As of December 31, 2015, the Company had 18,837,024 registered Preferred Shares issued and outstanding in share capital, which was comprised of (i) 440,001 Series A-1 Preferred Shares CHF 0.03 par value per share; (ii) 3,120,001 Series A-2 Preferred Shares, CHF 0.03 par value per share; (iii) 10,758,006 Series A-3 Preferred Shares, CHF 0.03 par value per share; and, (iv) 4,519,016 Series B Preferred Shares, CHF 0.03 par value per share, (collectively, the "Preferred Shares") .

The Company's redeemable convertible preferred shares were classified as temporary or mezzanine equity on the accompanying consolidated balance sheets in accordance with authoritative guidance for the classification and measurement of redeemable securities as the Preferred Shares are contingently redeemable at the option of the holders.

In April 2015, the Company issued 10,758,006 Series A-3 Preferred Shares in exchange for $4.24 per share whereby $2.12 per share was received upon issuance, resulting in gross proceeds of $22.8 million and the balance of $2.12 per share was due upon meeting certain milestones. As of December 31, 2015, none of the milestones had occurred and the Company had an outstanding subscription receivable of $22.8 million related to the Series A-3 Preferred Shares. In connection with the issuance of the Series A-3 Preferred Shares, the Company amended the dividend and conversion terms of the Series A-1 and Series A-2 Preferred Shares. The Company's policy requires the evaluation of amendments to equity classified preferred shares qualitatively to determine whether they are considered a modification or extinguishment. Based on this approach, the amendment to the terms of the Series A-1 and A-2 Preferred Shares was considered a modification and as a result, there was no adjustment to the carrying value of the Series A-1 and A-2 Preferred Shares. The balance of the Series A-3 Preferred Share subscription receivable of $2.12 per share was called on May 5, 2016 by the Board of Directors and gross proceeds of $22.8 million were received by May 27, 2016.

In May 2015, the Company issued 4,519,016 Series B Preferred Shares in exchange for CHF 6.20 ($6.74) per share resulting in gross proceeds of CHF 28.0 million ($30.5 million).

In January 2016, the Company issued 5,464,608 Series B Preferred Shares upon conversion of $38.4 million of Vertex Convertible Loans plus accrued interest and $35.0 million of Bayer Convertible Loans at a conversion price of $13.43 per share.

In June 2016, the Company issued 2,834,252 Series B Preferred Shares in exchange for $13.43 per share resulting in gross proceeds of $38.1 million.

11. Share Capital

The Company had 41,092,969 and 40,253,674 registered Common Shares as of December 31, 2017 and 2016, respectively, with a par value of CHF 0.03 per share. Included in the registered Common Shares as of December 31, 2017 is 55,848 shares of unvested restricted stock award and 444,873 treasury shares, which are legally outstanding, but are not considered outstanding for accounting purposes.

Conditional Capital Reserved for Future Issuance

The Company had the following conditional capital reserved for future issuance:

		As of December 31,	
Type of Share Capital	**Conditional Capital**	**2017**	**2016**
Common Shares	Unvested unissued restricted stock	166,667	166,667
Common Shares	Outstanding stock options	6,262,339	4,535,371
Common Shares	Reserved for future issuance under stock option plans (1)	4,657,700	5,290,643
Common Shares	Shares available for bonds and similar debt instruments	4,919,700	4,919,700
Common Shares	Shares available for employee purchase plans	413,226	413,226
	Total	16,419,632	15,325,607

(1) The Company's shareholders approved an increase to the option pool of 2,012,684 in May 2017.

Common Share Issuances

In October 2016, the Company completed an IPO whereby the Company sold 4,429,311 of its Common Shares, inclusive of 429,311 Common Shares sold by the Company pursuant to the partial exercise of an overallotment option granted to the underwriters in connection with the offering. Concurrent with the IPO, the Company issued and sold 2,500,000 Common Shares to Bayer BV, in a private placement. Additionally, the Company issued and subsequently reacquired the unexercised overallotment Common Shares of 170,689 at no cost, which are held in treasury.

In January 2018, the Company completed an offering of 5,750,000 shares of our common shares, which were sold at a price of $22.75 per share. This offering resulted in $122.6 million of net proceeds to the Company, refer to Note 17 "Subsequent Events," in the accompanying notes to the consolidated financial statements for further details.

The Common Shares have the following characteristics:

Voting Rights

The holders of Common Shares are entitled to one vote for each Common Share held at all meetings of shareholders and written actions in lieu of meetings.

Dividends

The holders of Common Shares are entitled to receive dividends, if and when declared by the Board of Directors. As of December 31, 2017, no dividends have been declared or paid since the Company's inception.

Liquidation

The holders of the Common Shares are entitled to share ratably in the Company's assets available for distribution to shareholders in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or upon the occurrence of a deemed liquidation event.

12. Equity-based Compensation

Option and Grant Plans

In July 2016, the shareholders approved the 2016 Share Option and Incentive Plan (the "2016 Plan") and in April 2015, the shareholders approved the 2015 option and grant plan (the "2015 Plan" collectively the "Plans"). Subsequent to the IPO, no further options shall be granted under the 2015 Plan. The Plans provide for the issuance of equity awards in the form of restricted shares, options to purchase Common Shares which may constitute incentive stock options ("ISOs") or non-statutory stock options ("NSOs"), unrestricted stock unit grants, and qualified performance and market-based awards to eligible employees, officers, directors, non-employee consultants, and other key personnel. Terms of the equity awards, including vesting requirements, are determined by the Board, subject to the provisions of the Plans. Options granted by the Company typically vest over four years and have a contractual life of ten years. The Company's Board of Directors approved an increase to the option pool of 2,012,684 options in May 2017.

During the years ended December 31, 2016 and 2015, the Company also issued outstanding Common Shares previously held by Founders and Fay Corp. to employees and non-employees as equity-based compensation ("Founder Awards"), which are subject to repurchase by the Company upon termination of the holder's service relationship with the Company as well as upon certain triggering events such as termination for cause, material breach of agreement and insolvency of the holder that generally lapse over a requisite service period of four years.

Equity-Based Compensation Expense

The Company uses the straight-line attribution method to recognize stock-based compensation expense for stock options and restricted stock awards. Stock options and restricted stock generally vests over four years with 25% vesting on the first anniversary, and the remaining vesting monthly thereafter. The following table presents stock-based compensation expense in the Company's Consolidated Statements of Operations:

	Years Ended December 31,		
	2017	2016	2015
Research and development	$ 8,800	$ 4,848	$ 1,924
General and administrative	10,073	5,844	1,760
Loss from equity method investment	1,763	152	—
Total	$ 20,636	$ 10,844	$ 3,684

Grant- Date Fair Value

The Company estimated the fair value of each employee and non-employee stock option award on the grant date using the Black-Scholes option-pricing model based on the following assumptions:

	Years Ended December 31,		
	2017	2016	2015
Employees:			
Options granted	2,894,850	2,411,240	1,913,319
Weighted - average exercise price	$ 16.92	$ 12.19	$ 2.32
Weighted-average grant date fair value	$ 10.86	$ 8.47	$ 3.11
Assumptions:			
Weighted-average expected volatility	72.1%	81.0%	76.4%
Expected term (in years)	6.0	6.0	6.0
Weighted-average risk free interest rate	2.0%	1.4%	1.7%
Expected dividend yield	0.0%	0.0%	0.0%
Non employees:			
Options granted	104,997	215,710	26,667
Weighted- average exercise price	$ 18.74	$ 19.54	$ 1.85
Weighted- average grant date fair value	$ 19.35	$ 17.38	$ 5.05
Assumptions:			
Weighted average expected volatility	81.5%	88.2%	84.1%
Expected term (in years)	9.4	10.0	10.0
Weighted-average risk free interest rate	2.4%	2.4%	2.2%
Expected dividend yield	0.0%	0.0%	0.0%

The fair value of the restricted stock awards was determined based on the fair value of Common Stock on the grant date. Non-employee stock options and restricted stock awards are marked-to-market at each reporting period.

Share Based Payment Activity

Stock Options

The following table summarizes stock option activity for employees and non-employees during the year ended December 31, 2017 (intrinsic value in thousands):

	Stock Options		Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)		Aggregate Intrinsic Value
Outstanding at December 31, 2016	4,535,371	$	8.38	9.1	$	53,975
Granted	2,999,847	$	16.98			
Exercised	(862,227)	$	3.53			
Cancelled or forfeited	(410,652)	$	7.06			
Outstanding at December 31, 2017	6,262,339	$	13.24	8.8		64,120
Exercisable at December 31, 2017	1,617,647	$	9.64	8.3	$	22,391
Vested or expected to vest at December 31, 2017 (1)	6,262,339	$	13.24	8.8	$	64,120

(1) This represents the number of vested stock options as of December 31, 2017 plus the unvested outstanding options at December 31, 2017 expected to vest in the future.

The total unrecognized compensation cost for employee and non-employee stock options is adjusted for estimated forfeitures. As of December 31, 2017, the Company expects to recognize total unrecognized compensation cost related to stock options of $42.2 million over a remaining weighted-average period of 3.4 years.

During 2017 and 2016, the Company granted options to purchase 60,000 and 123,333 Common Shares, respectively, subject to performance-based vesting conditions. As of December 31, 2017, options to purchase 362,872 Common Shares subject to performance-based vesting conditions were vested, as performance conditions were achieved, and there were no options to purchase Common Shares subject to performance-based vesting conditions outstanding. During 2017, the Company also granted 150,000 stock options with market-based vesting conditions in which the recipient is eligible to receive between zero and 150,000 options to purchase Common Shares at the end of a four year service period based upon achieving a specified average stock price. As of December 31, 2017, no options to purchase Common Shares subject to market-based vesting conditions were vested.

During the year ended December 31, 2017, the Chairman of the Board of Directors resigned. Coinciding with his resignation, he and the Company entered into an advisory agreement to perform consulting services. In consideration for performing consulting services, he was allowed to continue to vest in the options during the advisory period, with a post-termination exercise period of 150 days from the last day of the service relationship or the expiration of the option, whichever is earlier. The service relationship is expected to continue until September 10, 2019. Management determined that his services to be provided under the advisory agreement were not substantive. Therefore, the entire $2.2 million of compensation expense to be recognized prospectively was recognized immediately.

Restricted Stock

The following table summarizes restricted stock activity for employees and non-employees during the year ended December 31, 2017:

	Reflected as outstanding upon vesting	Reflected as outstanding upon grant date	Total		Weighted-Average Grant Date Fair Value
Unvested restricted common shares at December 31, 2016	89,367	650,856	740,223	$	3.84
Granted	101,667	—	101,667	$	17.45
Vested	(33,519)	(418,032)	(451,551)	$	6.40
Cancelled or forfeited	—	(23,938)	(23,938)	$	1.72
Unvested restricted common shares at December 31, 2017	157,515	208,886	366,401	$	8.49

During the years ended December 31, 2017 and 2016, the total fair value of restricted stock vested was $8.3 million and $9.9 million, respectively. At December 31, 2017, total unrecognized compensation expense related to unvested restricted stock was $3.6 million which the Company expects to recognize over a remaining weighted-average period of 1.3 years.

During the year ended December 31, 2016, the Company and Fay Corp. transferred 290,400 Common Shares to a founder, 268,093 of which are subject to vesting conditions with a weighted average grant date fair value of $12.65 per share. The unvested Common Shares are subject to repurchase by the Company upon termination of the holder's service relationship with the Company as well as upon certain triggering events such as termination for cause, material breach of agreement and insolvency of the holder. During the years ended December 31, 2017 and 2016, the Company recognized expense related to the Common Shares transferred to the Founder of $0.8 million and $2.6 million, respectively.

13. 401(k) Savings Plan

The Company established a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan") in November 2016. 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. The Company contributed $0.5 million to the 401(k) Plan for the year ended December 31, 2017.

14. Income Taxes

The Company is subject to U.S. federal and various state corporate income taxes as well as taxes in foreign jurisdictions for the foreign parent and where foreign subsidiaries have been established.

Net loss before taxes

For the years ended December 31, 2017, 2016 and 2015, the loss before provision for income taxes consist of the following (in thousands):

	Years Ended December 31,		
	2017	2016	2015
Domestic	$ 5,184	$ 3,322	$ 593
Foreign	(71,792)	(26,040)	(26,414)
Total	$ (66,608)	$ (22,718)	$ (25,821)

The (provision for) benefit from income taxes consist of the following (in thousands):

	Years Ended December 31,		
	2017	2016	2015
Current income taxes:			
Federal	$ (1,533)	$ (649)	$ (23)
State	(42)	11	(12)
Foreign	6	17	(26)
Total current income taxes	(1,569)	(621)	(61)
Deferred income taxes:			
Federal	(477)	30	(37)
State	297	105	65
Foreign	—	2	26
Total deferred income taxes	(180)	137	54
Total income tax provision	$ (1,749)	$ (484)	$ (7)

A reconciliation of income tax expense computed at the statutory corporate income tax rate to the effective income tax rate for the years ended December 31, 2017, 2016 and 2015 is as follows:

	Years Ended December 31,		
	2017	2016	2015
Income tax expense at statutory rate	9.3%	10.3%	10.3%
State income tax, net of federal benefit	0.3%	1.3%	0.1%
Nondeductible expenses	0.0%	1.6%	0.0%
Foreign rate differential	(2.5%)	(3.3%)	(1.4%)
Statutory to US GAAP permanent differences	1.8%	6.6%	0.0%
Stock-based compensation	(2.9%)	(4.9%)	(1.4%)
Research credits	0.8%	3.1%	0.6%
Change in valuation allowance	(9.4%)	(16.8%)	(8.2%)
Effective income tax rate	(2.6%)	(2.1%)	—

The federal statutory rate reflects the Switzerland mixed company service rate.

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. The significant components of the Company’s deferred tax assets are comprised of the following (in thousands):

	Years Ended December 31,	
	2017	2016
Deferred tax assets:		
Net operating loss carryforwards	$ 9,987	$ 3,934
Accruals and reserves	1,123	791
Deferred Rent	3,494	5,228
Other deferred tax assets	36	7
Deferred revenue	1,721	2,525
Research credit	543	425
Total deferred tax assets	16,904	12,910
Less valuation allowance	(13,041)	(6,770)
Net deferred tax assets	3,863	6,140
Deferred tax liabilities:		
Depreciation	(3,791)	(5,909)
Intangible assets	(59)	(68)
Other deferred tax liabilities	(31)	—
Total deferred tax liabilities	(3,881)	(5,977)
Long term deferred taxes	$ (18)	$ 163

The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on the Company’s history of operating losses in its non-U.S. jurisdictions, the Company has concluded that it is more-likely-than-not that the benefit of its non-U.S. deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance against its net deferred tax assets in Switzerland, and in the UK for its TRACR subsidiary, as of December 31, 2017 and 2016. The valuation allowance increased by $6.3 million during 2017, which is primarily attributable to losses in Switzerland. Additionally, the Company has established a valuation allowance for certain U.S. deferred tax assets.

On December 22, 2017, the Tax Cuts and Jobs Act ("the Act") was enacted in the United States. The Act reduces the U.S. federal corporate tax rate from 35% to 21%, requires companies 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. On December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act (“SAB 118”), which allows the recording of provisional amounts during a measurement period not to extend beyond one year of the enactment date. At December 31, 2017, the Company has assessed its provisional accounting for the tax effects of enactment of the Act, including the effects on our existing deferred tax balances and the one-time transition tax. For the year ended December 31, 2017, the Company has recognized no transition tax. The final impact may differ from this provisional amount due to, among other things, changes in interpretations and assumptions the Company has made thus far and the issuance of additional regulatory or other guidance. The Company expects to complete the final impact within the measurement period.

As a result of the Act, the Company remeasured certain deferred tax assets and liabilities based on the rates at which they are anticipated to reverse in the future, which is generally 21%. This resulted in a decrease to the Company's gross deferred tax assets of $0.2 million. The impact of the rate reduction on the Company's deferred tax assets and liabilities is provisional.

As of December 31, 2017, the Company had available non-U.S. net operating loss carryforwards of $127.4 million which begin to expire in 2020. As of December 31, 2017, the Company has U.S. domestic state research and development credit carryforwards of $0.4 million which begin to expire in 2032.

As of December 31, 2017, the Company has U.S. domestic federal research and development credit carryforwards of $0.3 million which expire in 2037, which are net of uncertain tax positions of $0.2 million.

ASC 740 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statement by prescribing the minimum recognition threshold and measurement of a tax position taken or expected to be taken in a tax return.

As of December 31, 2017 the Company had gross unrecognized tax benefits of $0.4 million of which $0.3 million would favorably impact the effective tax rate if recognized. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2017, 2016 and 2015, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's consolidated statements of operations and comprehensive loss.

The aggregate changes in gross unrecognized tax benefits was as follows (in thousands):

	Years Ended December 31,		
	2017	2016	2015
Balance at beginning of year	$ 163	$ 49	$ —
Increases for tax positions taken during current period	178	134	49
Increases for tax positions taken in prior periods	13	—	—
Decreases for tax positions taken during current period	—	—	—
Decreases for tax positions taken in prior periods	—	(20)	—
Balance at end of year	$ 354	$ 163	$ 49

The Company files income tax returns in the U.S. federal jurisdiction, Massachusetts, and certain non-U.S. jurisdictions. The Company is subject to U.S. federal, Massachusetts, and non-U.S. income tax examinations by authorities for all tax years.

15. Selected Quarterly Financial Data (Unaudited)

Prior to its IPO on October 18, 2016, the Company had outstanding participating Preferred Shares. During the fourth quarter of the year ended December 31, 2016, the Company had net income, although for the full year the Company had a net loss. Accordingly, the Company used the two-class method to calculate net income per share for the fourth quarter of 2016. For purposes of calculating basic net income per share for the fourth quarter of 2016, the Company excluded from the numerator $3.1 million of net income attributable to participating securities. The Company calculated diluted net income per share under both the if-converted method and the two-class method and concluded that the two-class method was more dilutive than the if-converted method. Accordingly, the two-class income allocations were reapplied after taking into account the dilutive effect of non-participating securities. This resulted in net income of $3.1 million being allocated to the participating securities and excluded from the numerator of the Common Stock dilutive net income per share calculation.

	2017			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Collaboration revenue	$ 2,703	$ 3,582	$ 2,387	$ 32,325
Total operating expenses	23,447	24,888	25,957	$ 31,353
(Loss) income from operations	(20,744)	(21,306)	(23,570)	$ 972
Net (loss) income	(21,475)	(22,315)	(24,707)	$ 140
Net (loss) income attributable to common shareholders	(21,475)	(22,315)	(24,707)	$ 140
Net (loss) income per share attributable to common shareholders:				
Basic	$ (0.54)	$ (0.56)	$ (0.62)	$ 0.00
Diluted	$ (0.54)	$ (0.56)	$ (0.62)	$ 0.00
Weighted-average common shares outstanding used in net (loss) income per share attributable to common shareholders:				
Basic	39,725,947	39,895,938	40,088,718	40,509,897
Diluted	39,725,947	39,895,938	40,088,718	41,635,843

	2016			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter (1)
Collaboration revenue	$ 476	$ 795	$ 1,549	$ 2,344
Total operating expenses	12,128	17,353	16,159	27,654
Loss from operations	(11,652)	(16,558)	(14,610)	(25,310)
Net (loss) income	(8,442)	(17,164)	(14,694)	17,098
Net (loss) income attributable to common shareholders	(8,439)	(17,157)	(14,680)	17,099
Net (loss) income per share attributable to common shareholders:				
Basic	$ (1.53)	$ (3.15)	$ (2.77)	$ 0.43
Diluted	$ (1.53)	$ (3.15)	$ (2.77)	$ 0.40
Weighted-average common shares outstanding used in net (loss) income per share attributable to common shareholders:				
Basic	5,528,079	5,448,855	5,292,348	32,987,335
Diluted	5,528,079	5,448,855	5,292,348	34,989,218

(1) During the fourth quarter the Company recorded an immaterial correction of an error of $1.2 million for rent expense related to the three months ended September 30, 2016. The Company determined that these errors are not material to the respective interim financial statements.

16. Related Party Transactions

The Company is a party to intellectual property license agreements with Dr. Charpentier. As of December 31, 2017, and December 31, 2016, the Company owed Dr. Charpentier approximately $0 and $0.5 million, respectively, of sublicense fees primarily related to the Bayer Agreement. During the year ended December 31, 2017, the Company did not record any sublicensing fees due to Dr. Charpentier in research and development expense related to the Bayer Agreement. During 2016, the Company recorded sublicensing fees of $1.0 million due to Dr. Charpentier in research and development expense related to the Bayer Agreement.

During the year ended December 31, 2017 and 2016, the Company recognized revenue of $4.8 million, and $1.1 million, respectively, related to the collaboration with Casebia. During the year ended December 31, 2017 and 2016, the Company recognized research and development expense of $4.5 million and $1.7 million, respectively, related to the performance of services for Casebia. The Company and Casebia have engaged several research institutions and companies to identify new delivery strategies and applications of the CRISPR/Cas9 technology. Additionally, the Company and Casebia are also a party to a number of research license agreements. The Company and Casebia will share costs associated with the research and license agreements. The Company received reimbursements of $4.4 million for both research and license agreements during 2017 which was recorded as a reduction of R&D expense in the income statement. There were no reimbursements recorded during 2016.

17. Subsequent Events

In January 2018, the Company completed an offering of 5,750,000 shares of our common shares, which were sold at a price of $22.75 per share. This offering resulted in $122.6 million of net proceeds to the Company. The underwriting discount of $7.8 million and other expenses of $0.4 million related to the equity offering were recorded as an offset to additional paid-in capital.

Casebia Therapeutics LLP and Subsidiary

Consolidated Financial Statements

As of December 31, 2017 and 2016, and for the Year ended December 31, 2017 and the Period From February 12, 2016 (Inception) Through December 31, 2016

Casebia Therapeutics LLP and subsidiary

Index to Consolidated Financial Statements

Report of Independent Auditors

The Board of Directors and Stockholders

Casebia Therapeutics LLP

We have audited the accompanying consolidated financial statements of Casebia Therapeutics LLP and subsidiary, which comprise the consolidated balance sheets as of December 31, 2017 and 2016, and the related consolidated statements of operations, comprehensive loss, changes in partners' equity, and cash flows for the year ended December 31, 2017 and for the period from February 12, 2016 (inception) through December 31, 2016, and the related consolidated notes to the consolidated financial statements.

Management's Responsibility for the Financial Statements

Management is responsible for the preparation and fair presentation of these financial statements in conformity with U.S. generally accepted accounting principles; this includes the design, implementation and maintenance of internal control relevant to the preparation and fair presentation of financial statements that are free of material misstatement, whether due to fraud or error.

Auditor's Responsibility

Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the financial statements. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatement of the financial statements, whether due to fraud or error. In making those risk assessments, the auditor considers internal control relevant to the entity's preparation and fair presentation of the financial statements in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the entity's internal control. Accordingly, we express no such opinion. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of significant accounting estimates made by management, as well as evaluating the overall presentation of the financial statements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Opinion

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Casebia Therapeutics LLP and subsidiary at December 31, 2017 and 2016, and the consolidated results of their operations and their cash flows for the year ended December 31, 2017 and for the period from February 12, 2016 (inception) through December 31, 2016 in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 8, 2018

Casebia Therapeutics LLP and subsidiary
Consolidated balance sheets

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 26,347,434	$ 2,216,490
Due from partners	1,330,405	—
Prepaid and other current assets	595,116	36,948
Tenant improvement allowance receivable	—	1,299,007
Total current assets	28,272,955	3,552,445
Property and equipment, net	9,906,893	4,560,488
Restricted cash	1,225,352	1,225,768
Other long-term assets	45,826	—
Total assets	$ 39,451,026	$ 9,338,701
Liabilities and Equity		
Current liabilities:		
Accounts payable	$ 1,224,805	$ 397,441
Due to partners	4,002,374	1,881,160
Deferred rent	590,426	722,977
Accrued expenses	2,792,859	302,137
Total current liabilities	8,610,464	3,303,715
Deferred rent	4,341,203	5,043,355
Total liabilities	12,951,667	8,347,070
Commitments and contingencies		
Partners' Equity:		
Partners' equity	26,499,359	60,991,631
Contribution receivable from partner	—	(60,000,000)
Total partners' equity	26,499,359	991,631
Total liabilities and partners' equity	$ 39,451,026	$ 9,338,701

See accompanying notes to consolidated financial statements.

Casebia Therapeutics LLP and subsidiary
Consolidated statements of operations and comprehensive loss

	Year ended December 31, 2017	Period from February 12, 2016 (inception) through December 31, 2016
Operating expenses:		
General and administrative	$ 9,672,302	$ 3,458,074
Research and development	26,607,443	77,373,590
Total operating expenses	36,279,745	80,831,664
Loss from operations	(36,279,745)	(80,831,664)
Other income:		
Interest income	57,806	—
Net loss and comprehensive loss	$ (36,221,939)	$ (80,831,664)

See accompanying notes to consolidated financial statements.

Casebia Therapeutics LLP and subsidiary
Consolidated statements of cash flows

	Year ended December 31, 2017	Period from February 12, 2016 (inception) through December 31, 2016
Cash flows from operating activities:		
Net loss	$ (36,221,939)	$ (80,831,664)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,007,915	7,329
Equity-based compensation expense	1,729,667	152,270
Non-cash contributions by partners	—	199,347
Deferred rent expense	28,260	374,132
Contribution of in-process research and development	—	36,371,678
Changes in operating assets and liabilities:		
Due from partners	(1,330,405)	—
Prepaid expenses	(558,168)	(36,948)
Other long-term assets	(45,826)	—
Accounts payable	546,620	372,258
Due to partners	2,121,214	1,881,160
Accrued expenses	2,495,722	297,137
Net cash used in operating activities	(30,226,940)	(41,213,301)
Cash flows from investing activities:		
Additions to property and equipment	(5,642,532)	(444,441)
Net cash used in investing activities	(5,642,532)	(444,441)
Cash flows from financing activities:		
Capital contributions from partners	60,000,000	45,100,000
Net cash provided by financing activities	60,000,000	45,100,000
Net increase in cash, cash equivalents and restricted cash	24,130,528	3,442,258
Cash, cash equivalents and restricted cash, beginning of period	3,442,258	—
Cash, cash equivalents and restricted cash, end of period	$ 27,572,786	$ 3,442,258
Non-cash investing activities:		
Purchases of property and equipment included in accounts payable and accrued expenses	$ 305,927	$ 30,183
Property and equipment additions acquired under tenant improvement allowance	$ 436,044	$ 4,093,193
Non-cash financing activities:		
Capital contribution receivable from partner	$ —	$ 60,000,000
Contribution of in-process research and development from partner	$ —	$ 36,371,678
Non-cash contributions from partners	$ —	$ 199,347

See accompanying notes to consolidated financial statements.

Casebia Therapeutics LLP and subsidiary
Consolidated statements of changes in partners' equity

	Partners' equity	Contribution receivable from partner	Total Partners' equity
Balance at February 12, 2016 (inception)	$ —	$ —	$ —
Contributions from partners	105,100,000	—	105,100,000
Contribution of in-process research and development from partner	36,371,678	—	36,371,678
Net loss	(80,831,664)	—	(80,831,664)
Partner equity-based compensation	152,270	—	152,270
Other non-cash contributions by partners	199,347	—	199,347
Contribution receivable from partner	—	(60,000,000)	(60,000,000)
Balance at December 31, 2016	$ 60,991,631	$ (60,000,000)	$ 991,631
Contributions from partners	—	60,000,000	60,000,000
Net loss	(36,221,939)	—	(36,221,939)
Partner equity-based compensation	1,729,667	—	1,729,667
Balance at December 31, 2017	$ 26,499,359	$ —	$ 26,499,359

See accompanying notes to consolidated financial statements.

1. Organization and Operations

Organization

Casebia Therapeutics LLP (the "JV" or "Casebia") is a joint venture formed between CRISPR Therapeutics AG ("CRISPR") and Bayer HealthCare LLC ("Bayer HealthCare") in February 2016 focused on discovering, developing and commercializing CRISPR/Cas9 gene-editing therapeutics to treat the genetic causes of bleeding disorders, autoimmune disease, blindness, hearing loss, heart disease and certain metabolic diseases.

Joint Venture Agreement

The Joint Venture Agreement between CRISPR and Bayer HealthCare (the "JV Agreement") was entered into on December 19, 2015. On February 12, 2016, CRISPR and Bayer HealthCare completed the formation of Casebia, a limited liability partnership formed in the United Kingdom. Casebia is a free-standing entity which has its own scientific leadership and management team. Casebia's Board of Directors has equal representation from Bayer HealthCare and CRISPR.

Bayer HealthCare and CRISPR each received a 50% partnership interest in the entity in exchange for their contributions to Casebia. At inception, CRISPR contributed $0.1 million in cash and licensed its proprietary CRISPR/Cas9 gene editing technology and intellectual property for selected disease indications. Bayer HealthCare contributed protein engineering expertise and relevant disease know-how. Bayer HealthCare has also committed to provide up to $300.0 million in research and development funding to Casebia over the first five years, subject to certain conditions. Under the joint venture agreement, CRISPR has no obligation to provide any additional funding and CRISPR's ownership interest will not be diluted from future contributions from Bayer.

CRISPR and Bayer HealthCare also provide compensated services to Casebia through separate agreements.

Under the JV Agreement, Casebia owed CRISPR $35.0 million in exchange for a worldwide, exclusive license to commercialize CRISPR's CRISPR/Cas9 technology specifically for the indications designated by Casebia. In March 2016, Casebia paid the first portion of the amount owed to CRISPR through a $20.0 million non-refundable technology access fee. The remaining $15.0 million non-refundable payment was made on December 22, 2016 following delivery of the consents necessary from patent holders of CRISPR's intellectual property. There are no milestone, royalty or other payments due to CRISPR under this aspect of the agreement.

The JV Agreement can be terminated by Bayer HealthCare and CRISPR upon mutual written consent. Either party may terminate the JV Agreement in the event of specified breaches by the other party or in the event the other party becomes subject to specified bankruptcy, winding up or similar circumstances. Either party may also terminate upon a change of control of the other party, as defined in the JV Agreement. Bayer HealthCare also has the right to terminate in the event (i) CRISPR is not able to maintain the intellectual property rights licensed to Casebia pursuant to the CRISPR IP Contribution Agreement or (ii) CRISPR has not achieved preclinical proof of concept with a CRISPR/Cas9 product candidate in a specified period of time.

The JV Agreement may also be terminated by either party if, subsequent to the time that Bayer HealthCare has funded its entire $300.0 million commitment, management is unable to approve and obtain sufficient funding, within the time specified in the JV Agreement, to continue Casebia's operations for the next 18 months.

Subject to certain exceptions, in the event of a termination, all Casebia owned patents, know-how and technology will be jointly owned by CRISPR and Bayer HealthCare, with the right to sublicense. Upon termination, subject to certain exceptions, Bayer HealthCare will receive an exclusive license to Casebia CRISPR/Cas technology for all non-human therapeutic uses in cardiology, hematology and ophthalmology (the "Bayer Fields") and a non-exclusive license for human therapeutic uses. Upon such termination, CRISPR will receive an exclusive license to Casebia CRISPR/Cas technology in human therapeutic areas, other than in the Bayer Fields, and a non-exclusive license for human therapeutic uses in the Bayer Fields. Upon any termination, all rights licensed to Casebia pursuant to the CRISPR IP Contribution Agreement will terminate, except for any rights licensed to third parties or to a party who has exercised an option pursuant to the Option Agreement described below.

In connection with the establishment the JV, Casebia, Bayer HealthCare and CRISPR entered into an Option Agreement. Pursuant to the Option Agreement, in the event the U.S. Food and Drug Administration accepts an Investigational New Drug application submitted by Casebia for any product candidate it is developing, both CRISPR and Bayer HealthCare have the right to submit an offer to enter into a license with Casebia for the exclusive right to develop, manufacture and commercialize the product candidate in certain specified fields. In addition, Casebia is allowed to receive and consider unsolicited third-party offers, and both CRISPR and Bayer HealthCare can require Casebia to seek third-party offers for the applicable product candidate. The Option Agreement sets forth the procedures the Board of Directors will follow when considering and voting on any offers as well as the considerations on how to value any offer.

Liquidity

The JV Agreement sets forth the initial 24-month budget for Casebia, which is revised by management on a yearly basis for the following 24 months. Bayer HealthCare, subject to certain conditions, is solely responsible for providing Casebia with the necessary additional funding until the earlier of (i) its aggregate remaining commitment is fully funded, at which point all additional financing must be approved by the Board of Directors or (ii) the termination of the JV Agreement in accordance with its terms.

Through December 31, 2017, Bayer HealthCare has contributed $105.0 million to Casebia. In January 2018, Bayer HealthCare made an additional capital contribution in the amount of $54.0 million to Casebia.

Casebia's net loss for 2017 was $36.2 million. As of December 31, 2017, Casebia had unrestricted cash and cash equivalents of $26.3 million. Casebia believes that its cash and cash equivalents as of December 31, 2017, along with the capital contribution received from Bayer HealthCare in January 2018, will be sufficient to fund its current operating plan for at least the next 12 months.

2. Summary of significant accounting policies

Basis of presentation and consolidation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"), and include the accounts of Casebia and its subsidiary. All intercompany accounts and transactions have been eliminated. 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 ("ASUs") of the Financial Accounting Standards Board ("FASB").

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, Casebia's management evaluates its estimates, which include, but are not limited to, equity-based compensation expense and reported amounts of expenses during the reporting period. In addition, significant estimates in these consolidated financial statements have been made in connection with the calculation of the value of contributed technology and research and development expenses. Casebia bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

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, or decision-making group, in deciding how to allocate resources and in assessing performance. Casebia's chief operating decision maker, the chief executive officer, views Casebia's operations and manages its business in one operating segment which is the business of discovering, developing and commercializing CRISPR/Cas9 gene-editing therapeutics in the licensed therapeutic areas.

Cash, cash equivalents and restricted cash

Casebia considers all highly liquid investments with maturities of 90 days or less from the purchase date to be cash equivalents. As of December 31, 2017, Casebia held $26.3 million in cash and cash equivalents, consisting of cash and money market funds. As of December 31, 2016, Casebia held $2.2 million in cash. All cash was held in depository accounts and is reported at fair value.

The following table reconciles cash, cash equivalents and restricted cash reported within Casebia's consolidated balance sheets to the total of the same amounts shown in the consolidated statements of cash flows:

	As of December 31, 2017	As of December 31, 2016
Cash and cash equivalents	$ 26,347,434	$ 2,216,490
Restricted cash	1,225,352	1,225,768
Total cash, cash equivalents and restricted cash shown in statement of cash flows	$ 27,572,786	$ 3,442,258

In April 2016, Casebia entered into a $1.2 million letter of credit to secure its obligations under a sublease. The letter of credit is secured by cash held in a restricted depository account.

Concentrations of Credit Risk and Off-balance Sheet Risk

Financial instruments that potentially subject Casebia to concentrations of credit risk are primarily cash and cash equivalents. Casebia's cash and cash equivalents are held in accounts with financial institutions that management believes are creditworthy. Casebia has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. Casebia has no financial instruments with off-balance sheet risk of loss.

Property and equipment

Property and equipment 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. Upon disposal, the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss is included in the results of operations. Depreciation is recorded using the straight-line method over the estimated useful lives of the respective assets, which are as follows:

Asset	Estimated useful life
Computer equipment	3 years
Furniture, fixtures, and other	5 years
Laboratory equipment	5 years
Leasehold improvements	Shorter of useful life or remaining lease term

Research and Development Expenses

Research and development costs, which include employee compensation costs, facilities, lab supplies and materials, overhead, preclinical development, and other related costs, are charged to expense as incurred.

Operating Leases

Casebia leases office and laboratory facilities under non-cancelable operating lease agreements. The lease agreements contain free or escalating rent payment provisions. Casebia recognizes rent expense under such leases on a straight-line basis over the term of the lease with the difference between the expense and the payments recorded as deferred rent on the consolidated balance sheets. Amounts received from lessors are accounted for as lease incentives, which are amortized as a reduction of rent expense over the term of the lease. Amounts received from lessees under subleases equal amounts owed under Casebia's original lease and are recognized on a straight-line basis as a reduction of rent expense over the term of the sublease. Lease renewal periods are considered on a lease-by-lease basis in determining the lease term.

Equity-based Compensation Expense

Certain employees of Casebia have been granted options to purchase CRISPR common stock. In accordance with FASB ASC Topic 323-10, Investments – Equity Method and Joint Ventures ("ASC 323-10"), CRISPR expenses the cost of the stock options granted to employees of Casebia as incurred. Concurrently, Casebia will also recognize the same cost of the stock options as an expense and capital contribution from CRISPR.

CRISPR accounts for stock options issued to non-employees under FASB ASC Topic 505-50, Equity-Based Payments to Non-Employees ("ASC 505-50"). As such, the value of such options is periodically remeasured and income or expense is recognized over their vesting terms. Compensation cost related to awards with service-based vesting schedules is recognized using the straight-line method. CRISPR estimates the fair value of stock options using the Black-Scholes option pricing model.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (i) the expected share price volatility, (ii) the calculation of expected term of the award, (iii) the risk-free interest rate and (iv) the expected dividend yield. Due to the lack of sufficient public market data for the trading of CRISPR's Common Shares and a lack of CRISPR-specific historical and implied volatility data, CRISPR has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The group of representative companies have characteristics similar to CRISPR, including stage of product development and focus on the life science industry. For options granted to non-employees, CRISPR utilizes the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. CRIPSR uses an assumed dividend yield of zero as CRISPR has never paid dividends and has no current plans to pay any dividends on its Common Shares.

CRISPR measures equity-based compensation awards granted to non-employees at fair value as the awards vest and recognizes the resulting value as compensation expense at each financial reporting period.

Patent Costs

Costs to secure and prosecute patent application and other legal costs related to the protection of Casebia's intellectual property are expensed as incurred, and are classified as general and administrative expenses in Casebia's consolidated statements of operations.

Income taxes

Casebia is a limited liability partnership. No provision for federal income taxes is necessary in the financial statements of Casebia because, as a partnership, it is not subject to federal income tax and the tax effect of its activities accrues to the partners.

In certain circumstances, partnerships may be held to be associations taxable as corporations. The Internal Revenue Service has issued regulations specifying circumstances under current law when such a finding may be made, and management has obtained an opinion of counsel based on those regulations that the partnership is not an association taxable as a corporation. A finding that the partnership is an association taxable as a corporation could have a material adverse effect on the financial position and results of operations of the partnership.

Fair value of financial instruments

Casebia's financial instruments consist of accounts payable and accrued expenses. Casebia is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. FASB ASC Topic 820, Fair Value Measurement and Disclosures ("ASC 820"), established a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available. Observable inputs are inputs that market participants would use in pricing the financial instrument based on market data obtained from sources independent of Casebia. Unobservable inputs are inputs that reflect Casebia's assumptions about the inputs that market participants would use in pricing the financial instrument and are developed based on the best information available in the circumstances.

The accounting standard describes a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value, which are the following:

Level 1 —Quoted prices in active markets that are accessible at the market date for identical unrestricted assets or liabilities.

Level 2 —Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs for which all significant inputs are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 —Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

To the extent that 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 Casebia 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.

Comprehensive Loss

Comprehensive loss consists of net loss and changes in equity during the period from transactions and other events and circumstances generated from non-owner sources. Casebia's net loss equals comprehensive loss for the year ended December 31, 2017 and the period from February 12, 2016 (inception) to December 31, 2016.

Subsequent Events

Casebia considers events or transactions that occur after the balance sheet date but prior to the date the financial statements are available to be issued for potential recognition or disclosure in the financial statements. Casebia has completed an evaluation of all subsequent events after the audited balance sheet date of December 31, 2017 through March 8, 2018, to ensure that these financial statements include appropriate disclosure of events recognized in the financial statements as of December 31, 2017, and events which occurred subsequently but were not recognized in the financial statements.

Recent Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606) ("ASU 2014-09"). Subsequently, the FASB also issued ASU No. 2015-14, Revenue from Contracts with Customers (Topic 606), which adjusted the effective date of ASU 2014-09; ASU No. 2016-08, Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations (Reporting Revenue Gross versus Net), which amends the principal-versus-agent implementation guidance and illustrations in ASU 2014-09; ASU No. 2016-10, Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing, which clarifies identifying performance obligation and licensing implementation guidance and illustrations in ASU 2014-09; and ASU No. 2016-12, Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients, which addresses implementation issues and is intended to reduce the cost and complexity of applying the new revenue standard in ASU 2014-09 (collectively, the "Revenue ASUs").

The Revenue ASUs noted above provide an accounting standard for a single comprehensive model for use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance. The accounting standard is effective for interim and annual periods beginning after December 15, 2017, with an option to early adopt for interim and annual periods beginning after December 15, 2016. The guidance permits two methods of adoption: retrospectively to each prior reporting period presented (the full retrospective method), or retrospectively with the cumulative effect of initially applying the guidance recognized at the date of initial application (the modified retrospective method). Casebia currently anticipates adoption of the new standard effective January 1, 2018 under the full retrospective method. Casebia does not expect the adoption of ASU 2014-09 to have an effect on its consolidated financial statements as it does not currently have any revenue generating arrangements.

In August 2014, the FASB issued ASU No. 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's ability to Continue as a Going Concern ("ASU 2014-15"), which requires management to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. This guidance is effective for the annual reporting period ending after December 15, 2016 and for annual and interim periods thereafter. Casebia adopted ASU 2014-15 on December 31, 2016 and its adoption did not have an effect on its consolidated financial statements or disclosures.

In February 2016, the FASB issued ASU No. 2016-02, Leases ("ASU 2016-02"), which applies to all leases and will require lessees to record most leases on the balance sheet, but recognize expense in a manner similar to the current standard. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018 and interim periods within those years, which is the year ended December 31, 2019 for Casebia. Entities are required to use a modified retrospective approach of adoption for leases that exist or are entered into after the beginning of the earliest comparative period in the financial statements, with certain practical expedients available. Casebia is evaluating the new guidance and the expected effect on its consolidated financial statements.

In March 2016, the FASB issued ASU No. 2016-09, Compensation—Stock Compensation (Topic 718) ("ASU 2016-09"). The guidance changes how companies account for certain aspects of equity-based payments to employees. Entities will be required to recognize income tax effects of awards in the income statement when the awards vest or are settled. The guidance also allows an employer to repurchase more of an employee's shares than it can under current guidance for tax withholding purposes providing for withholding at the employee's maximum rate as opposed to the minimum rate without triggering liability accounting and to make a policy election to account for forfeitures as they occur. CRISPR adopted the new standard January 1, 2017. CRISPR made an accounting policy election to account for the impact of pre-vesting forfeitures as they occur rather than applying an estimated forfeiture rate, as previously required. Adoption did not materially impact Casebia's consolidated financial statements.

In November 2016, the FASB issued ASU No. 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash ("ASU 2016-18"). ASU 2016-18 requires that a statement of cash flows explain the change during the period in the total cash, cash equivalents, and amounts generally described as restricted cash or restricted cash equivalents. Therefore, amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning and ending balances shown on the statement of cash flows. The guidance is effective for annual periods beginning after December 15, 2017 and early adoption is permitted. ASU 2016-18 must be applied retrospectively to all periods presented. Casebia adopted ASU 2016-18 as of January 1, 2017. The 2016 period in Casebia's statements of cash flows reflects an increase in operating cash flows from the increase in restricted cash during 2016. Casebia does not expect any additional impact on its financial statements.

In January 2017, the FASB issued ASU No. 2017-01, *Business Combinations* (Topic 805) ("ASU 2017-01"). ASU 2017-01 clarifies whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The purpose of the guidance is to narrow the definition of a business at it relates recording transactions as business acquisitions or asset acquisitions. The guidance is effective in annual periods beginning after December 15, 2017, including interim periods within those years, with early adoption permitted under certain circumstances. Casebia does not expect any additional impact on its financial statements.

3. **Fair Value Measurements**

The fair value measurements of the Casebia's financial instruments at December 31, 2017 is summarized in the table below:

	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Balance at December 31, 2017
Assets:				
Money market funds	$ 26,347,434	$ —	$ —	$ 26,347,434
Restricted cash	1,225,352	—	—	1,225,352
Total	$ 27,572,786	$ —	$ —	$ 27,572,786

The fair value measurements of the Casebia's financial instruments at December 31, 2016 is summarized in the table below:

	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Balance at December 31, 2016
Assets:				
Cash	$ 2,216,490	$ —	$ —	$ 2,216,490
Restricted cash	1,225,768	—	—	1,225,768
Total	$ 3,442,258	$ —	$ —	$ 3,442,258

The carrying amounts of due from partners, due to partners, accounts payable and accrued expenses as reported in the consolidated balance sheets as of December 31, 2017 and 2016 approximate fair value due to the short-term duration of these instruments. Casebia may elect to measure financial instruments and certain other items at specified election dates in the future.

The fair value of the CRISPR license which was written off following the formation of Casebia was calculated based on the consideration paid and the fair value of CRISPR's 50% interest in Casebia as of February 12, 2016, which was determined utilizing discounted cash flows based on reasonable estimates and assumptions of cash flows expected from Casebia, and thus considered a Level 3 input. The value of the intellectual property contributed by CRISPR was determined to be $36.4 million.

4. Property and Equipment, net

Property and equipment, net, consists of the following:

	As of December 31, 2017	As of December 31, 2016
Leasehold improvements	$ 7,560,655	$ —
Laboratory equipment	2,495,309	151,828
Furniture and fixtures	676,254	—
Computer hardware	189,919	15,562
Construction work in process	—	4,400,427
	10,922,137	4,567,817
Accumulated Depreciation	(1,015,244)	(7,329)
Property and equipment, net	$ 9,906,893	$ 4,560,488

Depreciation expense for the year ended December 31, 2017 and the period from February 12, 2016 (inception) through December 31, 2016 was $1.0 million and $7,329, respectively.

5. Accrued Expenses

Accrued expenses consist of the following:

	As of December 31, 2017	As of December 31, 2016
Payroll and employee-related costs	$ 1,536,368	$ 76,699
Collaboration expenses	935,000	—
Professional services	290,491	225,438
Other accrued expenses	31,000	—
Total	$ 2,792,859	$ 302,137

6. Commitments and Contingencies

Operating Leases

In August 2016, Casebia entered into an agreement with Pfizer, Inc. to sublease 32,688 square feet of office and laboratory space in Cambridge, MA. The sublease commenced in October 2016, expires in March 2024 and includes a tenant improvement allowance of $5.4 million. Of this tenant improvement allowance, $1.3 million and $4.1 million were recognized as leasehold improvements during the year ended December 31, 2017 and the period from February 12, 2016 (inception) to December 31, 2016. Casebia has the option to extend the term of the sublease by five years.

In May 2017, Casebia entered into an agreement to sublease 5,184 square feet of Casebia's office space in Cambridge, MA to Bayer HealthCare at a monthly rent per square foot equal to Casebia's monthly rent per square foot due to Pfizer. The sub-sublease was effective in May 2017 and expires in March 2024. Approximately $0.8 million of Casebia's tenant improvement allowance was allocated to improvements in the square footage occupied by Bayer. In addition, Bayer HealthCare has agreed to reimburse Casebia for approximately $1.0 million in leasehold improvements previously paid for by Casebia in excess of the tenant improvement allowance. As of December 31, 2017, Bayer HealthCare owed Casebia approximately $1.3 million under the terms of this sub-sublease, including outstanding rent and reimbursements for leasehold improvements and operating expenses, which is included in Due from Partners in the accompanying consolidated balance sheet.

In April 2017, Casebia entered into an agreement with Bayer HealthCare to sublease 7,036 square feet of office and laboratory space in San Francisco, CA. The sublease was effective in January 2017 and expires in December 2019. Casebia has the option to extend the term of the sublease by one year. In September 2017, Casebia entered into an amendment to increase the square footage under the sublease to 7,191, effective October 2017.

The future minimum payments for non-cancelable leases, net of non-cancelable sublease payments, for all non-cancelable operating leases as of December 31, 2017 is as follows:

	Lease Commitments	Sublease Income	Obligations, net of sublease income
Year Ending December 31,			
2018	$ 2,953,490	$ (397,597)	$ 2,555,893
2019	3,039,732	(409,534)	2,630,198
2020	2,659,577	(421,835)	2,237,742
2021	2,739,418	(434,498)	2,304,920
2022	2,821,546	(447,525)	2,374,021
Thereafter	3,638,093	(577,037)	3,061,056
Total	$ 17,851,856	$ (2,688,026)	$ 15,163,830

During 2016 Casebia occupied a portion of CRISPR's and Bayer HealthCare's office and laboratory space, for which Casebia was not charged rent. Casebia estimated noncash expense for these spaces of $9,792, which is recorded as Non-Cash Contributions from Partners in the accompanying consolidated statements of changes in partners' equity.

From January to April 2017 Casebia occupied a portion of CRISPR's office and laboratory space on a month-to-month basis.

Total rent expense for the year ended December 31, 2017 and the period from February 12, 2016 (inception) through December 31, 2016, net of sublease income, was $2,043,222 and $383,924.

7. Research Agreements

Seattle Children's Research Institute

In September 2017, Casebia entered into an exclusive license agreement and research collaboration with Seattle Children's Research Institute ("SCRI") to explore new methods to treat and prevent autoimmune disease using CRISPR/Cas9 gene-edited regulatory T cells ("Tregs") – a type of white blood cell that controls and modulates the body's immune response. Casebia will receive worldwide rights to develop and commercialize specific intellectual property related to the collaboration.

In exchange for the license, Casebia is also liable for annual maintenance fees of up to $350,000 per year under certain conditions. In addition, Casebia is obligated to make payments following the achievement of specific milestones of approximately $12.0 million. Following the first sale, if any, of a licensed product Casebia is obligated to pay royalties at a low single digit percentage of net sales of licensed products. Casebia has made no milestone or royalty payments to date under this agreement. Casebia recorded a total of $1.6 million of research and development expenses during the year ended December 31, 2017.

Other Agreements

Casebia is also a party to a number of research license agreements which require upfront payments, future royalty payments and potential milestone payments from time to time which could be significant. Casebia has recorded expense of $3.9 million and made payments of $2.1 million during the year ended December 31, 2017 related to these agreements. The difference of $1.8 million is included in Due to Partners in the accompanying consolidated balance sheets. In addition, Casebia has committed to making payments for related research and development services of $1.3 million in 2018 and $0.1 million in 2019.

8. Equity-based Compensation

Certain employees of Casebia have been granted options to purchase CRISPR common stock. Terms of the equity awards, including vesting requirements, are determined by CRISPR's Board of Directors, subject to the provisions of CRISPR's stock option plans. Options granted by CRISPR typically vest over four years and have a contractual life of ten years. In accordance with ASC 323-10, CRISPR expenses the cost of the stock options granted to employees of Casebia as incurred. CRISPR accounts for these options in accordance with ASC 505-50. As such, the value of such options is periodically remeasured and income or expense and is recognized by CRISPR over their vesting terms. Concurrently, Casebia will also recognize the same cost of the stock options as expense and a capital contribution from CRISPR. Compensation cost related to awards with service-based vesting schedules is recognized using the straight-line method.

Equity-based Compensation Expense

Total equity-based compensation expense is recognized for stock options granted to employees and has been reported in Casebia's consolidated statement of operations as follows:

	Year ended December 31, 2017	Period from February 12, 2016 (inception) through December 31, 2016
General and administrative	$ 1,069,483	$ 55,153
Research and development	660,184	97,117
Total	$ 1,729,667	$ 152,270

For equity awards that have previously been modified, any incremental increase in the fair value over the original award has been recorded as compensation expense on the date of the modification for vested awards or over the remaining service (vesting) period for unvested awards. For the year ended December 31, 2017, Casebia recorded $0.2 million of stock-based compensation expense related to modifications of stock options. The incremental compensation cost is the excess of the fair value of the modified award on the date of the modification over the fair value of the original award immediately before the modification.

Stock Option Awards

The following table summarizes stock option activity for CRISPR stock options granted to employees of Casebia:

	Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value
Outstanding at December 31, 2016	336,353	$ 13.19	9.5	$ 2,377,144
Granted	104,997	18.74		
Exercised	(70,380)	1.81		
Cancelled or forfeited	(45,237)	1.81		
Outstanding at December 31, 2017	325,733	$ 19.01	9.1	$ 1,457,406
Exercisable at December 31, 2017	70,983	$ 18.75	8.9	$ 335,997
Vested or expected to vest at December 31, 2017(1)	325,733	$ 19.01	9.1	$ 1,457,406

(1) Represents the number of vested options at December 31, 2017 plus the number of unvested options expected to vest based on the unvested options outstanding at December 31, 2017.

The fair value of options vested for the year ended December 31, 2017 and the period from February 12, 2016 (inception) through December 31, 2016 was $1.6 million and $0.2 million, respectively. The intrinsic value of options exercised for the year ended December 31, 2017 and the period from February 12, 2016 (inception) through December 31, 2016 was $1.2 million and zero, respectively. The weighted-average grant date fair values of stock options granted during the year ended December 31, 2017 and the period from February 12, 2016 (inception) through December 31, 2016 was $19.35 and $18.17, respectively.

As of December 31, 2017, the total unrecognized compensation cost related to CRISPR stock options was $4.5 million. The total unrecognized compensation cost will be adjusted for future forfeitures. As of December 31, 2017, Casebia expects to recognize total unrecognized compensation cost over a remaining weighted-average period of 3.0 years.

CRISPR estimates the fair value of each stock award on the grant date using the Black-Scholes option-pricing model based on the following range of assumptions regarding the fair value of the underlying Common Shares on each measurement date:

	Year ended December 31, 2017	Period from February 12, 2016 (inception) through December 31, 2016
Weighted average expected volatility	81.5%	88.2%
Expected term (in years)	9.4	9.5
Risk free interest rate	2.4%	2.3%
Expected dividend yield	0.0%	0.0%

9. Incentive Compensation Plans

Aspire 2.0 Plan

Certain Casebia executives are eligible to participate in Casebia’s Aspire 2.0 long-term incentive plan. Beginning in 2017, on January 1 of each year, participating employees receive an award based on a percentage of their salary in virtual shares of Bayer AG. These awards vest three years after the date of grant. Upon vesting of the awards, participants receive a cash payout based on the trading price of Bayer AGs stock for the last 30 days of the vesting period, including dividends.

Casebia will revalue these awards utilizing the share price of Bayer AG common stock at each reporting period through the remaining vesting period. The revaluation may result in additional charges to expense in the future.

Total compensation expense recognized for awards granted to employees has been reported in Casebia's consolidated statement of operations as follows:

		Year ended December 31, 2017
General and administrative	$	216,718
Research and development		—
Total	$	216,718

Casebia Liquidity Event Plan

During 2017, Casebia established a Liquidity Event Plan for its employees under which participants are eligible to receive a cash award in the event Casebia experiences a change in control, as defined, or an Initial Public Offering, under certain conditions. The cash awards would be paid out over an 18-month period, or immediately if the participant's position is eliminated due to the Liquidity Event. Casebia will recognize expense for awards under this plan when a Liquidity Event is deemed probable over the requisite service period. Given the inherent uncertainty of such transactions, a Liquidity Event would not be deemed probable until the closure of a relevant transaction. For the year ended December 31, 2017, none of the clincal and regulatory milestones were deemed probably and therefore, Casebia recorded no expense under the Liquidity Event Plan.

Casebia Long-term Incentive Plan

During 2017, Casebia established a Long-term Incentive Plan for its employees under which participants are eligible to receive a cash award upon the achievement of certain clinical and regulatory milestones. Casebia will recognize expense for awards under this plan as the relevant milestones are deemed probable. For the year ended December 31, 2017, Casebia recorded no expense under the Long-term Incentive Plan.

10. Related Party Transactions

An affiliate of Bayer HealthCare has agreed to provide to Casebia certain protein engineering knowhow as well as other administrative services, as detailed below. $1.0 million and $1.1 million of these expenses are included in Due to Partners in the accompanying balance sheet at December 31, 2017 and 2016, respectively. Bayer HealthCare provided management services to Casebia during 2016 that were not billed to Casebia. These expenses, totaling $189,555, were treated as a capital contribution in the accompanying financial statements.

CRISPR has also agreed to provide Casebia with certain general and administrative and research and development services, as detailed below. $2.6 million and $0.8 million of these expenses are included in Due to Partners in the accompanying balance sheet at December 31, 2017 and 2016, respectively. CRISPR and Casebia also share equally in certain in-license fees with third parties.

During 2017, Casebia employees were covered under CRISPRs medical and other benefit plans. As of December 31, 2017, $398,062 was included in Due to Partners in the accompanying balance sheet under this arrangement, representing premium and other payments made by CRISPR on behalf of Casebia.

All amounts due to Partners are due within 30 days of receipt of the respective invoices.

Total related party expenses have been reported in Casebia's consolidated statement of operations as follows:

	Year ended December 31, 2017	Period from February 12, 2016 (inception) through December 31, 2016
General and administrative:		
Bayer AG and subsidiaries:		
Consulting services	$ —	$ 1,061,992
Rent, net of sublease income	71,172	1,250
Recruiting services	51,517	—
Total Bayer	122,689	1,063,242
CRISPR:		
Administrative services	—	90,712
Rent	6,289	3,542
Total CRISPR	6,289	94,254
Total general and administrative	$ 128,978	$ 1,157,496
Research and development:		
Bayer AG and subsidiaries:		
Research services	$ 3,996,384	$ 3,788,565
Rent, net of sublease income	79,706	3,750
Total Bayer	4,076,090	3,792,315
CRISPR:		
Research services	4,280,233	1,086,406
In-license cost sharing	3,865,750	—
Rent	7,044	1,250
Total CRISPR	8,153,027	1,087,656
Total research and development	$ 12,229,117	$ 4,879,971

11. Income Taxes

Casebia is a pass-through entity for federal and state income tax purposes and generally is not subject to income taxes. Instead, its earnings and losses are included in the income tax returns of the partners.

12. Employee Benefit Plan

Casebia maintains a defined contribution 401(k) plan (the "Plan") in which substantially all of its permanent employees are eligible to participate. Employee contributions are voluntary and are determined on an individual basis, limited by the maximum amounts allowable under federal tax regulations. Casebia makes matching contributions of 100% of the first 3% and 50% of the next 2% of employees' contributions to the Plan. Casebia recorded employer contribution expense of $168,995 and $2,622 for the year ended December 31, 2017 and the period from February 12, 2016 (inception) through December 31, 2016, respectively.

Exhibit 10.13

EMPLOYMENT AGREEMENT

This Employment Agreement ("Agreement") is made as of the 13th day of November, 2017, between CRISPR Therapeutics, Inc., a Delaware corporation (the "Company"'), and Michael Tomsicek (the "Executive" and, together with the Company, the "Parties" or each individually, a "Party").

WHEREAS, the Company is a wholly owned subsidiary of CRISPR Therapeutics AG ("Parent" or "CRISPR AG"): and

WHEREAS, Parent and the Company are each subject to the Swiss Ordinance act against excessive compensation in listed companies as a result of the of listing of the common shares of Parent on the NASDAQ Global Market.

NOW, THEREFORE, in consideration of the mutual covenants and agreements herein contained and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties agree as follows:

NOW, THEREFORE, in consideration of the mutual covenants and agreements herein contained and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties agree as follows:

1. Position and Duties. The employment of the Executive by the Company will commence on the date hereof. The Executive will serve as the Senior Vice President, Chief Financial Officer of the Company. The Executive shall have responsibilities and duties consistent with such position and such other responsibilities and duties as may from time to time be prescribed by the Chief Executive Officer of the Company (the "CEO") which are not inconsistent with the Executive's skills and experience or his ability to discharge his responsibilities in the positions noted above. The Executive shall devote the Executive's full working time and efforts to the business and affairs of the Company except as otherwise permitted under Section 3(b)(i). Notwithstanding the foregoing, the Executive may engage in charitable or other community activities, as long as such services and activities are disclosed to the Board of Directors of Parent (the "Board") and do not materially interfere with the Executive's performance of the Executive's duties to the Company as provided in this Agreement. During the period which the Executive is employed pursuant to this Agreement (the "Employment Period"), the Executive's principal place of employment will be in the Greater Boston, Massachusetts area; however, the Company may require the Executive to travel temporarily to other locations in connection with the Company's business.

2. Compensation and Related Matters.

(a) Base Salary. During the Employment Period, the Company shall pay the Executive, as compensation for the performance of the Executive's duties and obligations under this Agreement, an annual base salary of $380,000, payable in a manner that is consistent with the Company's usual payroll practices for senior executives. The Executive's base salary shall be reviewed annually by each of the Compensation Committee of the Board or any successor to such committee (the "Committee") and the Board or for adjustment. Such adjustment, if any, shall be within the sole discretion of the Board. The annual base salary in effect at any given time is referred to herein as "Base Salary."

(b) Annual Bonus. During the Employment Period, the Executive shall be eligible to receive an annual target bonus (a "Bonus") if, as reasonably determined by the Board or, to the extent delegated by the Board, the Committee one or more of the performance targets annually determined by the Board or the Committee ("Performance Targets") is achieved. If all of the Performance Targets are achieved, the Bonus will equal not less than 40 percent of the Executive's Base Salary (the "Target Bonus"). In the event that less than all of the Performance Targets are met by Executive, the Bonus paid in respect of this paragraph may be less than the Target Bonus. Except as set forth in Section 5(a) hereof, the Executive must be employed by the Company on the day any such earned Bonus is paid which shall be not later than 2 ½ months after the end of each calendar year. The Executive's target bonus opportunity as a percentage of Base Salary may be reviewed periodically and adjusted in the sole discretion of the Board. After any such adjustment, the term "Target Bonus" shall refer to the increased amount.

(c) Equity Compensation. The Executive shall be eligible to participate in Parent's equity incentive plan according to its terms and conditions, as defined by Parent from time to time in its sole discretion. Both entitlement to any equity awards and the amount shall be determined by Parent in its sole discretion.

(d) Expenses. During the Employment Period, the Executive shall be entitled to receive reimbursement for all reasonable expenses incurred by him in performing services hereunder, in accordance with the policies and procedures then in effect and established by the Company for its senior executive officers.

(e) Other Benefits. During the Employment Period, the Executive shall be entitled to participate in or receive benefits under any employee benefit plan or arrangement currently maintained or which may, in the future, be made available by the Company generally to its executives and key management employees, subject to and on a basis consistent with the terms, conditions and overall administration of such plan or arrangement. Any payments or benefits payable to the Executive under a plan or arrangement referred to in this Section 2(e) in respect of any calendar year during which the Executive is employed by the Company for less than the whole of such year shall, unless otherwise provided in the applicable plan or arrangement, be prorated in accordance with the number of days in such calendar year during which the Executive is so employed. Should any such payments or benefits accrue on a fiscal (rather than calendar) year, then the proration in the preceding sentence shall be on the basis of a fiscal year rather than calendar year.

(f) Vacations. The Executive shall be entitled to accrue up to 20 paid vacation days in each year, which shall be accrued ratably. In other respects, the Company's vacation policy as the same may then be in effect shall apply to vacations.

(g) Approval by Shareholders' Meeting and Mandatory Law. Any compensation (including bonus, equity awards and fringe benefits) to be paid under this

Agreement, is, to the extent required by Swiss laws and the Parent's Article of Association, subject to approval by the general meeting of shareholders' of Parent. In the event of a conflict between this Agreement and applicable mandatory Swiss law, the Company shall have the right to unilaterally modify the Agreement to the extent necessary to comply with mandatory law with immediate effect.

(h) Lost Opportunity Compensation. To offset losses the Executive incurred in connection with the transitioning of his employment to the Company, the Company will make a one-time payment to the Executive in the amount of $50,000 in the first payroll after January 1, 2018. This payment is subject to the usual required withholdings. The Executive understands and agrees that, in the event his employment with the Company is terminated for any reason prior to November 12, 2018, he will reimburse the Company, within one (1) month after such employment termination, for this full amount ($50,000). The Executive further agrees that such amount may be collected by the Company, either directly or indirectly, from any (i) payment of any kind due to the Executive from the Company or any affiliate thereof including, without limitation, accrued wages, vacation, final wages, and expense reimbursements to the fullest extent permitted by applicable law; and/or (ii) the forfeiture or cancellation of any equity interest owned by the Executive in the Parent, the Company or any subsidiary or affiliate thereof, whether now existing or hereafter formed, and regardless of the form such equity interest.

3. Termination.

(a) General. The Executive's employment shall continue until it is terminated in accordance with this Agreement. Upon service of a Notice of Termination (as defined below), the Executive shall resign from all offices and functions assumed in relation to this Agreement effective upon first request of the Company.

(b) Termination by the Company without Cause or by Executive for Good Reason: Notice Period. In the event that the Company elects to terminate the Executive's employment without Cause (as defined below) or the Executive elects to resign from Executive's employment with Good Reason (as defined below) (in either case an "Involuntary Departure"), the Party electing to end the employment relationship shall provide the other Party with a Notice of Termination (as defined below) of the Involuntary Departure specifying a notice period (the "Notice Period") of six (6) months, effective as per the end of a calendar month; provided that, in the case that the Notice of Termination of an Involuntary Departure is provided within the 12 month period following a Change in Control (the "Change in Control Period" or "CIC Period"), then the Notice Period shall be 12 months.

(i) During the Notice Period following a Notice of Termination of an Involuntary Departure, the Executive shall continue to be available to provide services to the extent requested by the Company or the Board, provided at any time during the Notice Period the Company may replace the Executive's position and/or direct the Executive to perform other or reduced work; provided further that, upon the 15th day following such Notice of Termination (or such earlier date as the Company shall determine in its sole discretion), the Company shall release the Executive from his working obligations pursuant to Section 3(b)(i) (except to the extent the parties otherwise agree) and place the Executive on garden leave for the remainder of the Notice Period

(“Garden Leave”). During such Garden Leave, the Executive (A) may enter into consulting arrangements and accept board positions provided such outside business activities do not interfere with Executive’s obligations under this Agreement including without limitation, pursuant to Section 7 and (B) shall be free to engage in other employment provided that such employment does not interfere with Executive’s obligations under this Agreement including without limitation, pursuant to Section 7. The Company shall be prohibited during the Garden Leave from reducing any compensation to which the Executive is entitled to receive during the remainder of the Notice Period pursuant to Section 3(b)(ii).

(ii) With respect to compensation during the Notice Period following a Notice of Termination of an Involuntary Departure, and subject to (i) the Executive signing, within 30 days following the date that the Notice of Termination is given, a Release of Claims in a form reasonably required by the Company (the “Release”) and (ii) Section 6, the Executive: (A) shall continue to receive the Base Salary and employee benefits consistent with the Company’s then existing benefits plans and programs; (B) shall be entitled to receive an amount equal to the Target Bonus with respect to the Notice Period (i.e., a prorated Target Bonus based upon the number of days in the applicable Notice Period), which amount shall be payable no more than 60 days after the Notice of Termination (provided that if the 60-day period begins in one calendar year and ends in a second calendar year, such Target Bonus shall be paid in the second calendar year); (C) shall continue to vest through the last day of the Notice Period in any [time based] equity awards outstanding as of the date the Notice of Termination is given; provided, and notwithstanding the foregoing, Section 5(a) may apply if the Notice of Termination of an Involuntary Departure occurs during a CIC Period, and (D) shall not continue to accrue vacation under Section 2(f).

(iii) If during the Notice Period following a Notice of Termination of an Involuntary Departure, the Company terminates the Executive’s employment for Cause, then the Company shall provide a restated Notice of Termination and the Notice Period shall end on the earlier date set forth in the restated Notice of Termination.

(c) Death. The Executive’s employment hereunder shall terminate upon his death.

(d) Disability. The Company may terminate the Executive’s employment if the Executive is disabled and unable to perform the essential functions of the Executive’s then existing position or positions with or without reasonable accommodation for a period of 180 days (which need not be consecutive) in any 12-month period. If any question shall arise as to whether during any period the Executive is disabled so as to be unable to perform the essential functions of the Executive’s then existing position or positions with or without reasonable accommodation, the Executive may, and at the request of the Company shall, submit to the Company a certification in reasonable detail by a physician selected by the Company to whom the Executive or the Executive’s guardian shall have no reasonable objection as to whether the Executive is so disabled or how long such disability is expected to continue, and such certification shall for the purposes of this Agreement be conclusive of the issue. The Executive shall cooperate with any reasonable request of the physician in connection with such certification. If such question shall arise and the Executive shall fail to submit such certification, the Company's determination of such issue shall be binding on the Executive. Nothing in this Section 3(d) shall be construed to waive the Executive's rights, if any, under existing law including, without limitation, the Family and Medical Leave Act of 1993, 29 U.S.C. §2601 *et seq.* and the Americans with Disabilities Act, 42 U.S.C. §12101 *et seq.*

(e) Termination by Company for Cause. The Company may terminate the Executive's employment hereunder for Cause.

(f) Termination by the Executive Without Good Reason. The Executive may terminate her employment hereunder at any time without Good Reason.

(g) Definitions:

(i) Cause. For purposes of this Agreement, "Cause" shall mean: (i) the Executive's commission of any felony or commission of any crime involving fraud, dishonesty or moral turpitude; (ii) the Executive's commission or attempted commission of or participation in a fraud or act of dishonesty against the Company; (iii) the Executive's material breach of any contract or agreement between the Executive and the Company or the Executive's material breach of any legal duty he owes to the Company; (iv) conduct by the Executive that constitutes insubordination, incompetence or neglect of duties; (v) the Executive's failure to perform the duties, functions and responsibilities of the Executive's position; or (vi) the Executive's failure to cooperate with a bona fide internal investigation or an investigation by regulatory or law enforcement authorities, after being instructed by the Company to cooperate, or the willful destruction or failure to preserve documents or other materials known to be relevant to such investigation or the inducement of others to fail to cooperate or to produce documents or other materials in connection with such investigation; provided, however, the actions or conduct described in clauses (iv) and (v) above shall only constitute Cause if the Company provides the Executive with written notice thereof and the Executive has not, within 30 days of receipt such written notice, discontinued the cited conduct or remedied the failure to perform and further provided that lawful actions taken by the Executive in the exercise of his rights under the United States Constitution shall not constitute a breach of subsection (vi) above.

(ii) Good Reason. For purposes of this Agreement, "Good Reason" shall mean that the Executive has complied with the "Good Reason Process" (hereinafter defined) following the occurrence of any of the following events: (i) a material diminution in the Executive's responsibilities, authority and function, an adverse change to Executive's job title, or a change in Executive's reporting relationship that results in the Executive no longer reporting directly to the CEO; (ii) a material reduction in Base Salary except pursuant to a salary reduction program affecting substantially all of the employees of the Company, provided that it does not adversely affect the Executive to a greater extent than other similarly situated employees; (iii) a material change in the principal geographic location at which the Executive provides services to the Company outside of the Greater Boston, Massachusetts area; or (iv) the material breach of this Agreement by the Company (each a "Good Reason Condition"). Good Reason Process shall mean that (i) the Executive reasonably determines in good faith that a Good Reason Condition has occurred; (ii) the Executive notifies the Company in writing of the first occurrence of the Good Reason Condition within 60 days of the occurrence of such condition; (iii) the Executive cooperates in good faith with the Company's efforts, for a period not less than 30 days following such notice (the "Cure Period"), to remedy the Good Reason Condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) the Executive terminates employment within 60 days after the end of the Cure Period. If the Company cures the Good Reason Condition during the Cure Period, Good Reason shall be deemed not to have occurred.

(iii) Notice of Termination. Except for termination as specified in Section 3(c), any termination of the Executive's employment by either the Company or the Executive shall be communicated by written Notice of Termination to the other party hereto. For purposes of this Agreement, a "Notice of Termination" shall mean a notice which shall indicate the specific termination provision in this Agreement relied upon.

(iv) Date of Termination. For purposes of this Agreement, "Date of Termination" shall mean: (i) if the Executive's employment is terminated by death, the date of death; (ii) if the Executive's employment is terminated on account of disability under Section 3(d) or by the Company for Cause under Section 3(e), the date on which Notice of Termination is given; (iii) if the Executive's employment terminates as a result of an Involuntary Departure under Section 3(b), the last day of the Notice Period; (iv) if the Executive's employment is terminated by the Executive under Section 3(f) without Good Reason, 30 days after the date on which a Notice of Termination is given (unless the Company waives all or part of the thirty (30) day period).

4. Compensation Upon Termination. If the Executive's employment with the Company is terminated for any reason, the Company shall pay or provide to the Executive (or to the Executive's authorized representative or estate) (i) any Base Salary earned through the Date of Termination; (ii) unpaid expense reimbursements (subject to, and in accordance with Section 2(d) of this Agreement); (iii) subject to Section 3(b)(ii)(D), unused vacation that accrued through the Date of Termination; and (iv) any vested benefits the Executive may have under any employee benefit plan of the Company through the Date of Termination, which vested benefits shall be paid and/or provided in accordance with the terms of such employee benefit plans (together, the "Accrued Benefit") on or before the time required by law but in no event more than 30 days after the Executive's Date of Termination.

5. Change in Control.

(a) Acceleration of Vesting. In the event a Notice of Termination of an Involuntary Termination occurs during the CIC Period, and subject to the Executive signing, within 60 days following the Notice of Termination, a Release and the Release becoming effective and non-revocable within such 60-day period, all time based stock options and time based stock-based awards held by the Executive as of the date of the Notice of Termination, shall vest and become exercisable or nonforfeitable. Notwithstanding the foregoing, if, at the time of a Change in Control, the Company determines in its sole discretion, in reliance upon an opinion of counsel in form and substance satisfactory to the Company, that the acceleration in the prior sentence would not be permissible under applicable law, then in lieu of the acceleration in the prior sentence, all time based stock options and time based stock-based awards held by the Executive as of the date of such Change in Control, shall vest and become exercisable or nonforfeitable as of the date of such Change in Control.

(b) Excise Tax.

(i) Anything in this Agreement to the contrary notwithstanding, in the event that any compensation, payment or distribution by the Company to or for the benefit of the Executive, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise (the "Parachute Payments"), would be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), the following provisions shall apply:

(A) If the Parachute Payments, reduced by the sum of (1) the Excise Tax and (2) the total of the Federal, state, and local income and employment taxes payable by the Executive on the amount of the Parachute Payments which are in excess of the Threshold Amount, are greater than or equal to the Threshold Amount, the Executive shall be entitled to the full benefits payable under this Agreement.

(B) If the Threshold Amount is less than (x) the Parachute Payments, but greater than (y) the Parachute Payments reduced by the sum of (1) the Excise Tax and (2) the total of the Federal, state, and local income and employment taxes on the amount of the Parachute Payments which are in excess of the Threshold Amount, then the Parachute Payments shall be reduced (but not below zero) to the extent necessary so that the sum of all Parachute Payments shall not exceed the Threshold Amount. In such event, the Parachute Payments shall be reduced in the following order: (1) cash payments not subject to Section 409A of the Code; (2) cash payments subject to Section 409A of the Code; (3) equity-based payments and acceleration; and (4) non-cash forms of benefits. To the extent any payment is to be made over time (*e.g.*, in installments, etc.), then the payments shall be reduced in reverse chronological order.

(ii) For the purposes of this Section 5(c), "Threshold Amount" shall mean three times the Executive's "base amount" within the meaning of Section 280G(b)(3) of the Code and the regulations promulgated thereunder less one dollar ($1.00); and "Excise Tax" shall mean the excise tax imposed by Section 4999 of the Code, and any interest or penalties incurred by the Executive with respect to such excise tax.

(iii) All calculations and determinations under Sections 5(c)(i) and 5(c)(ii) shall be made by an independent accounting firm or independent tax counsel appointed by the Company (the "Tax Counsel") whose determinations shall be conclusive and binding on the Company and the Executive for all purposes. For purposes of making the calculations and determinations required by Sections 5(c)(i) and 5(c)(ii), the Tax Counsel may rely on reasonable, good faith assumptions and approximations concerning the application of Section 280G and Section 4999 of the Code. The Company and the Executive shall furnish the Tax Counsel with such information and documents as the Tax Counsel may reasonably request in order to make its determinations under Sections 5(c)(i) and 5(c)(ii). The Company shall bear all costs the Tax Counsel may reasonably incur in connection with its services.

(c) Definitions. For purposes of this Section 5, "Change in Control" shall mean any of the following:

(i) any "person," as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended (the "Act") (other than Parent, any of its subsidiaries, or any trustee, fiduciary or other person or entity holding securities under any employee benefit plan or trust of Parent or any of its subsidiaries), together with all "affiliates" and "associates" (as such terms are defined in Rule 12b-2 under the Act) of such person, shall become the "beneficial owner" (as such term is defined in Rule 13d-3 under the Act), directly or indirectly, of securities of Parent representing 50 percent or more of the combined voting power of the Company's then outstanding securities having the right to vote in an election of the Board ("Voting Securities") (in such case other than as a result of an acquisition of securities directly from Parent); or

(ii) the date a majority of the members of the Board is replaced during any 12-month period by directors whose appointment or election is not endorsed by a majority of the members of the Board before the date of the appointment or election; or

(iii) the consummation of (A) any consolidation or merger of Parent where the stockholders of Parent, immediately prior to the consolidation or merger, would not, immediately after the consolidation or merger, beneficially own (as such term is defined in Rule 13d-3 under the Act), directly or indirectly, shares representing in the aggregate more than 50 percent of the voting shares of the company issuing cash or securities in the consolidation or merger (or of its ultimate parent corporation, if any), or (B) any sale or other transfer (in one transaction or a series of transactions contemplated or arranged by any party as a single plan) of all or substantially all of the assets of Parent.

Notwithstanding the foregoing, a "Change in Control" shall not be deemed to have occurred for purposes of the foregoing clause (i) solely as the result of an acquisition of securities by Parent which, by reducing the number of shares of Voting Securities outstanding, increases the proportionate number of Voting Securities beneficially owned by any person to 50 percent or more of the combined voting power of all of the then outstanding Voting Securities; provided, however, that if any person referred to in this sentence shall thereafter become the beneficial owner of any additional shares of Voting Securities (other than pursuant to a stock split, stock dividend, or similar transaction or as a result of an acquisition of securities directly from Parent) and immediately thereafter beneficially owns 50 percent or more of the combined voting power of all of the then outstanding Voting Securities, then a "Change in Control" shall be deemed to have occurred for purposes of the foregoing clause (i). For the avoidance of doubt, a migratory merger of Parent for the principal purpose of redomiciling Parent shall not constitute a Change in Control.

6. Section 409A.

(a) Anything in this Agreement to the contrary notwithstanding, if at the time of the Executive's separation from service within the meaning of Section 409A of the Code, the Company determines that the Executive is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that the Executive becomes entitled to under this Agreement on account of the Executive's separation from service would be considered deferred compensation subject to the 20 percent additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) six months and one day after the Executive's separation from service, or (B) the Executive's death. If any such delayed cash payment is otherwise payable on an installment basis, the first payment shall include a catch-up payment covering amounts that would otherwise have been paid during the six-month period but for the application of this provision, and the balance of the installments shall be payable in accordance with their original schedule. Solely for purposes of Section 409A of the Code, each installment payment under this Agreement is considered a separate payment.

(b) All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by the Executive during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year. Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

(c) To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon the Executive's termination of employment, then such payments or benefits shall be payable only upon the Executive's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h).

(d) The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. The parties agree that this Agreement may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party.

(e) The Company makes no representation or warranty and shall have no liability to the Executive or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

7. Proprietary Information, Noncompetition and Cooperation.

(a) Restrictive Covenants and Assignment of Inventions. The Executive has entered into the Proprietary Information and Inventions Agreement (the "Confidentiality and Assignment Agreement"), attached hereto as Exhibit A, and agrees to continue to honor the obligations and restrictive covenants set forth in the Confidentiality and Assignment Agreement, the terms of which are incorporated by reference as material terms of this Agreement.

(b) Non-Competition and Non-Solicitation. In order to protect the Company's proprietary information and good will, during the Executive's employment with the Company and for a period of twelve (12) months following the (i) the delivery of a Notice of Termination, in the case of an Involuntary Departure or (ii) the termination of the Executive's employment for any other reason (the "Restricted Period"), the Executive will not directly or indirectly, whether as owner, partner, shareholder, director, manager, consultant, agent, employee, co-venturer or otherwise, engage, participate or invest in any Competing Business. For purposes hereof, the term "Competing Business" shall mean any entity engaged in the discovery, development or commercialization of CAS9 technology for human therapeutics. Notwithstanding the foregoing, nothing contained hereinabove or hereinbelow shall be deemed to prohibit the Executive from (i) acquiring, solely as an investment, shares of capital stock (or other interests) of any corporation (or other entity) not exceeding 2% of such corporation's (or other entity's) then outstanding shares of capital stock (or equity interest), or (ii) working for a line of business, division or unit of a larger entity that competes with the Company as long as the Executive's activities for such line of business, division or unit do not involve work by the Executive on matters that are directly competitive with the Company's business. In addition, during the Restricted Period, the Executive will not, directly or indirectly, in any manner, other than for the benefit of the Company (i) divert or take away customers of the Company or any of its suppliers; and/or (ii) solicit, entice, attempt to persuade any other employee or consultant of the Company to leave the Company for any reason (other than the termination of subordinate employees undertaken in the course of the Executive's employment with the Company). The Executive acknowledges and agrees that if the Executive violates any of the provisions of this paragraph 7(b), the running of the Restricted Period will be extended by the time during which the Executive engages in such violation(s).

(c) Litigation and Regulatory Cooperation. During and after the Executive's employment, the Executive shall use reasonable efforts to cooperate with the Company in the defense or prosecution of any claims or actions now in existence or that may be brought in the future against or on behalf of the Company that relate to events or occurrences that transpired while the Executive was employed by the Company. The Executive's cooperation in connection with such claims or actions shall include, but not be limited to, being available to meet with counsel to prepare for discovery or trial and to act as a witness on behalf of the Company at mutually convenient times. During and after the Executive's employment, the Executive shall use reasonable efforts to cooperate with the Company in connection with any investigation or review of any federal, state or local regulatory authority as any such investigation or review relates to events or occurrences that transpired while the Executive was employed by the Company. The Company shall reimburse the Executive for any reasonable out-of-pocket expenses incurred in connection with the Executive's performance of obligations pursuant to this Section 7(c).

(d) Injunction. The Executive agrees that it would be difficult to measure any damages caused to the Company that might result from any breach by the Executive of the promises set forth in this Section 7 and the Confidentiality and Assignment Agreement, and that in any event money damages would be an inadequate remedy for any such breach. Accordingly, subject to Section 8 of this Agreement, the Executive agrees that if the Executive breaches, or proposes to breach, any portion of this Agreement and the Confidentiality and Assignment Agreement, the Company shall be entitled, in addition to all other remedies that it may have, to an injunction or other appropriate equitable relief to restrain any such breach without showing or proving any actual damage to the Company.

(e) Protected Reporting; Defend Trade Secrets Act Immunity. Nothing in this Agreement or the Confidentiality and Assignment Agreement, and nothing in any policy or procedure, in any other confidentiality, employment, separation agreement or in any other document or communication from the Company limits the Executive's ability to file a charge or complaint with any government agency concerning any acts or omissions that the Executive may believe constitute a possible violation of federal or state law or making other disclosures that are protected under the whistleblower provisions of applicable federal or state law regulation or affects the Executive's ability to communicate with any government agency or otherwise participate in any investigation or proceeding that may be conducted by a government agency, including by providing documents or other information, without notice to the Company. In addition, for the avoidance of doubt, pursuant to the federal Defend Trade Secrets Act of 2016, the Executive shall not be held criminally or civilly liable under any federal or state trade secret law for the disclosure of a trade secret that (i) is made (A) in confidence to a federal, state, or local government official, either directly or indirectly, or to an attorney; and (B) solely for the purpose of reporting or investigating a suspected violation of law; or (ii) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal.

8. Arbitration of Disputes. Any controversy or claim arising out of or relating to this Agreement or the breach thereof or otherwise arising out of the Executive's employment or the termination of that employment (including, without limitation, any claims of unlawful employment discrimination whether based on age or otherwise) shall, to the fullest extent permitted by law, be settled by arbitration in any forum and form agreed upon by the parties or, in the absence of such an agreement, under the auspices of the American Arbitration Association ("AAA") in Boston, Massachusetts in accordance with the Employment Arbitration Rules of the AAA, including, but not limited to, the rules and procedures applicable to the selection of arbitrators. In the event that any person or entity other than the Executive or the Company may be a party with regard to any such controversy or claim, such controversy or claim shall be submitted to arbitration subject to such other person or entity's agreement. Judgment upon the award rendered by the arbitrator may be entered in any court having jurisdiction thereof. This Section 8 shall be specifically enforceable. Notwithstanding the foregoing, this Section 8 shall not preclude either party from pursuing a court action for the sole purpose of obtaining a

temporary restraining order or a preliminary injunction in circumstances in which such relief is appropriate; provided that any other relief shall be pursued through an arbitration proceeding pursuant to this Section 8.

9. Consent to Jurisdiction. To the extent that any court action is permitted consistent with or to enforce Section 8 of this Agreement, the parties hereby agree that the Middlesex County Superior Court of The Commonwealth of Massachusetts shall have exclusive jurisdiction of such dispute. Accordingly, with respect to any such court action, the Executive submits to the personal jurisdiction of such courts.

10. Integration. This Agreement and the Confidentiality and Assignment Agreement constitutes the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior agreements between the Parties concerning such subject matter.

11. Withholding. All payments made by the Company to the Executive under this Agreement shall be net of any tax or other amounts required to be withheld by the Company under applicable law.

12. Successor to the Executive. This Agreement shall inure to the benefit of and be enforceable by the Executive's personal representatives, executors, administrators, heirs, distributees, devisees and legatees. In the event of the Executive's death after her termination of employment but prior to the completion by the Company of all payments due him under this Agreement, the Company shall continue such payments to the Executive's beneficiary designated in writing to the Company prior to her death (or to her estate, if the Executive fails to make such designation).

13. Enforceability. If any portion or provision of this Agreement (including, without limitation, any portion or provision of any section of this Agreement) shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

14. Survival. The provisions of this Agreement and the Confidentiality and Assignment Agreement shall survive the termination of this Agreement and/or the termination of the Executive's employment to the extent necessary to effectuate the terms contained herein.

15. Waiver. No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of any party to require the performance of any term or obligation of this Agreement, or the waiver by any party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

16. Notices. Any notices, requests, demands and other communications provided for by this Agreement shall be sufficient if in writing and delivered in person or sent by a nationally recognized overnight courier service or by registered or certified mail, postage prepaid, return receipt requested, to the Executive at the last address the Executive has filed in writing with the

Company or, in the case of the Company, at its main offices, attention of the CEO and a copy of such notice shall be sent to Crispr AG, Attention: Chief Financial Officer, at the main offices of Crispr AG.

17. Amendment. This Agreement may be amended or modified only by a written instrument signed by the Executive and by a duly authorized representative of the Company.

18. Governing Law. This is a Massachusetts contract and shall be construed under and be governed in all respects by the laws of the Commonwealth of Massachusetts, without giving effect to the conflict of laws principles of such Commonwealth. With respect to any disputes concerning federal law, such disputes shall be determined in accordance with the law as it would be interpreted and applied by the United States Court of Appeals for the First Circuit.

19. Counterparts. This Agreement may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original; but such counterparts shall together constitute one and the same document.

20. Assignment and Transfer by the Company. The Company will have the right to assign and/or transfer this Agreement to its affiliates, successors and assigns. The Executive expressly consents to be bound by the provisions of this Agreement for the benefit of the Company or any parent, subsidiary or affiliate to whose employ the Executive may be transferred without the necessity that this Agreement be re-signed at the time of such transfer.

[Remainder of page intentionally left blank. Signature page follows.]

IN WITNESS WHEREOF, the parties have executed this Agreement effective on the date and year first above written.

CRISPR THERAPEUTICS, INC.

By: /s/ Rodger Novak

EXECUTIVE

Michael Tomsicek/s/ Michael Tomsicek

EXHIBIT A
Proprietary Information and Inventions Agreement

Exhibit 10.16

EMPLOYMENT AGREEMENT

This Employment Agreement ("Agreement") is made as of the 31st day of May, 2017, between CRISPR Therapeutics, Inc., a Delaware corporation (the "Company"), and James R. Kasinger (the "Executive" and, together with the Company, the "Parties" or each individually, a "Party").

WHEREAS, the Company is a wholly owned subsidiary of CRISPR Therapeutics AG ("Parent" or "CRISPR AG"): and

WHEREAS, Parent and the Company are each subject to the Swiss Ordinance act against excessive compensation in listed companies as a result of the of listing of the common shares of Parent on the NASDAQ Global Market.

NOW, THEREFORE, in consideration of the mutual covenants and agreements herein contained and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties agree as follows:

NOW, THEREFORE, in consideration of the mutual covenants and agreements herein contained and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties agree as follows:

1. Position and Duties. The employment of the Executive by the Company will commence on the date hereof. The Executive will serve as the General Counsel and Secretary of the Company. The Executive shall have responsibilities and duties consistent with such position and such other responsibilities and duties as may from time to time be prescribed by the Chief Executive Officer of the Company (the "CEO") which are not inconsistent with the Executive's skills and experience or his ability to discharge his responsibilities in the positions noted above. The Executive shall devote the Executive's full working time and efforts to the business and affairs of the Company except as otherwise permitted under Section 3(b)(i). Notwithstanding the foregoing, the Executive may engage in charitable or other community activities, as long as such services and activities are disclosed to the Board of Directors of Parent (the "Board") and do not materially interfere with the Executive's performance of the Executive's duties to the Company as provided in this Agreement. During the period which the Executive is employed pursuant to this Agreement (the "Employment Period"), the Executive's principal place of employment will be in the Greater Boston, Massachusetts area; however, the Company may require the Executive to travel temporarily to other locations in connection with the Company's business.

2. Compensation and Related Matters.

(a) Base Salary. During the Employment Period, the Company shall pay the Executive, as compensation for the performance of the Executive's duties and obligations under this Agreement, an annual base salary of $350,000, payable in a manner that is consistent with the Company's usual payroll practices for senior executives. The Executive's base salary shall be reviewed annually by each of the Compensation Committee of the Board or any successor to such committee (the "Committee") and the Board or for adjustment. Such adjustment, if any, shall be within the sole discretion of the Board. The annual base salary in effect at any given time is referred to herein as "Base Salary."

(b) Annual Bonus. During the Employment Period, the Executive shall be eligible to receive an annual target bonus (a "Bonus") if, as reasonably determined by the Board or, to the extent delegated by the Board, the Committee one or more of the performance targets annually determined by the Board or the Committee ("Performance Targets") is achieved. If all of the Performance Targets are achieved, the Bonus will equal not less than 40 percent of the Executive's Base Salary (the "Target Bonus"). In the event that less than all of the Performance Targets are met by Executive, the Bonus paid in respect of this paragraph may be less than the Target Bonus. Except as set forth in Section 5(a) hereof, the Executive must be employed by the Company on the day any such earned Bonus is paid which shall be not later than 2½ months after the end of each calendar year. The Executive's target bonus opportunity as a percentage of Base Salary may be reviewed periodically and adjusted in the sole discretion of the Board. After any such adjustment, the term "Target Bonus" shall refer to the increased amount.

(c) Equity Compensation. The Executive shall be eligible to participate in Parent's equity incentive plan according to its terms and conditions, as defined by Parent from time to time in its sole discretion. Both entitlement to any equity awards and the amount shall be determined by Parent in its sole discretion.

(d) Expenses. During the Employment Period, the Executive shall be entitled to receive reimbursement for all reasonable expenses incurred by him in performing services hereunder, in accordance with the policies and procedures then in effect and established by the Company for its senior executive officers.

(e) Other Benefits. During the Employment Period, the Executive shall be entitled to participate in or receive benefits under any employee benefit plan or arrangement currently maintained or which may, in the future, be made available by the Company generally to its executives and key management employees, subject to and on a basis consistent with the terms, conditions and overall administration of such plan or arrangement. Any payments or benefits payable to the Executive under a plan or arrangement referred to in this Section 2(e) in respect of any calendar year during which the Executive is employed by the Company for less than the whole of such year shall, unless otherwise provided in the applicable plan or arrangement, be prorated in accordance with the number of days in such calendar year during which the Executive is so employed. Should any such payments or benefits accrue on a fiscal (rather than calendar) year, then the proration in the preceding sentence shall be on the basis of a fiscal year rather than calendar year.

(f) Vacations. The Executive shall be entitled to accrue up to 20 paid vacation days in each year, which shall be accrued ratably. In other respects, the Company's vacation policy as the same may then be in effect shall apply to vacations.

(g) Approval by Shareholders' Meeting and Mandatory Law. Any compensation (including bonus, equity awards and fringe benefits) to be paid under this Agreement, is, to the extent required by Swiss laws and the Parent's Article of Association, subject to approval by the general meeting of shareholders' of Parent. In the event of a conflict between this Agreement and applicable mandatory Swiss law, the Company shall have the right to unilaterally modify the Agreement to the extent necessary to comply with mandatory law with immediate effect.

(h) Lost Opportunity Compensation. To offset losses the Executive incurred in connection with the transitioning of his employment to the Company, the Company will make a one-time payment to the Executive in the amount of $30,000 not later than the 45th day from the effective date of this Agreement. This payment is subject to the usual required withholdings. The Executive understands and agrees that, in the event his employment with the Company is terminated for any reason prior to June 1, 2018, he will reimburse the Company, within one (1) month after such employment termination, for this full amount ($30,000). The Executive further agrees that such amount may be collected by the Company, either directly or indirectly, from any (i) payment of any kind due to the Executive from the Company or any affiliate thereof including, without limitation, accrued wages, vacation, final wages, and expense reimbursements to the fullest extent permitted by applicable law; and/or (ii) the forfeiture or cancellation of any equity interest owned by the Executive in the Parent, the Company or any subsidiary or affiliate thereof, whether now existing or hereafter formed, and regardless of the form such equity interest.

3. Termination.

(a) General. The Executive's employment shall continue until it is terminated in accordance with this Agreement. Upon service of a Notice of Termination (as defined below), the Executive shall resign from all offices and functions assumed in relation to this Agreement effective upon first request of the Company.

(b) Termination by the Company without Cause or by Executive for Good Reason; Notice Period. In the event that the Company elects to terminate the Executive's employment without Cause (as defined below) or the Executive elects to resign from Executive's employment with Good Reason (as defined below) (in either case an "Involuntary Departure"), the Party electing to end the employment relationship shall provide the other Party with a Notice of Termination (as defined below) of the Involuntary Departure specifying a notice period (the "Notice Period") of six (6) months, effective as per the end of a calendar month; provided that, in the case that the Notice of Termination of an Involuntary Departure is provided within the 12 month period following a Change in Control (the "Change in Control Period" or "CIC Period"), then the Notice Period shall be 12 months.

(i) During the Notice Period following a Notice of Termination of an Involuntary Departure, the Executive shall continue to be available to provide services to the extent requested by the Company or the Board, provided at any time during the Notice Period the Company may replace the Executive's position and/or direct the Executive to perform other or reduced work; provided further that, upon the 15th day following such Notice of Termination (or such earlier date as the Company shall determine in its sole discretion), the Company shall release the Executive from his working obligations pursuant to Section 3(b)(i) (except to the extent the parties otherwise agree) and place the Executive on garden leave for the remainder of the Notice Period ("Garden Leave"). During such Garden Leave, the Executive (A) may enter into consulting arrangements and accept board positions provided such outside business activities do not interfere with Executive's obligations under this Agreement including without limitation, pursuant to Section 7 and (B) shall be free to engage in other employment provided that such employment does not interfere with Executive's obligations under this Agreement including without limitation, pursuant to Section 7. The Company shall be prohibited during the Garden Leave from reducing any compensation to which the Executive is entitled to receive during the remainder of the Notice Period pursuant to Section 3(b)(ii).

(ii) With respect to compensation during the Notice Period following a Notice of Termination of an Involuntary Departure, and subject to (i) the Executive signing, within 30 days following the date that the Notice of Termination is given, a Release of Claims in a form reasonably required by the Company (the "Release") and (ii) Section 6, the Executive: (A) shall continue to receive the Base Salary and employee benefits consistent with the Company's then existing benefits plans and programs; (B) shall be entitled to receive an amount equal to the Target Bonus with respect to the Notice Period (i.e., a prorated Target Bonus based upon the number of days in the applicable Notice Period), which amount shall be payable no more than 60 days after the Notice of Termination (provided that if the 60-day period begins in one calendar year and ends in a second calendar year, such Target Bonus shall be paid in the second calendar year); (C) shall continue to vest through the last day of the Notice Period in any [time based] equity awards outstanding as of the date the Notice of Termination is given; provided, and notwithstanding the foregoing, Section 5(a) may apply if the Notice of Termination of an Involuntary Departure occurs during a CIC Period, and (D) shall not continue to accrue vacation under Section 2(f).

(iii) If during the Notice Period following a Notice of Termination of an Involuntary Departure, the Company terminates the Executive's employment for Cause, then the Company shall provide a restated Notice of Termination and the Notice Period shall end on the earlier date set forth in the restated Notice of Termination.

(c) Death. The Executive's employment hereunder shall terminate upon his death.

(d) Disability. The Company may terminate the Executive's employment if the Executive is disabled and unable to perform the essential functions of the Executive's then existing position or positions with or without reasonable accommodation for a period of 180 days (which need not be consecutive) in any 12-month period. If any question shall arise as to whether during any period the Executive is disabled so as to be unable to perform the essential functions of the Executive's then existing position or positions with or without reasonable accommodation, the Executive may, and at the request of the Company shall, submit to the Company a certification in reasonable detail by a physician selected by the Company to whom the Executive or the Executive's guardian shall have no reasonable objection as to whether the Executive is so disabled or how long such disability is expected to continue, and such certification shall for the purposes of this Agreement be conclusive of the issue. The Executive shall cooperate with any reasonable request of the physician in connection with such certification. If such question shall arise and the Executive shall fail to submit such certification, the Company's determination of such issue shall be binding on the Executive.

Nothing in this Section 3(d) shall be construed to waive the Executive's rights, if any, under existing law including, without limitation, the Family and Medical Leave Act of 1993, 29 U.S.C. §2601 *et seq.* and the Americans with Disabilities Act, 42 U.S.C. §12101 *et seq.*

(e) Termination by Company for Cause. The Company may terminate the Executive's employment hereunder for Cause.

(f) Termination by the Executive Without Good Reason. The Executive may terminate her employment hereunder at any time without Good Reason.

(g) Definitions:

(i) Cause. For purposes of this Agreement, "Cause" shall mean: (i) the Executive's commission of any felony or commission of any crime involving fraud, dishonesty or moral turpitude; (ii) the Executive's commission or attempted commission of or participation in a fraud or act of dishonesty against the Company; (iii) the Executive's material breach of any contract or agreement between the Executive and the Company or the Executive's material breach of any legal duty he owes to the Company; (iv) conduct by the Executive that constitutes insubordination, incompetence or neglect of duties; (v) the Executive's failure to perform the duties, functions and responsibilities of the Executive's position; or (vi) the Executive's failure to cooperate with a bona fide internal investigation or an investigation by regulatory or law enforcement authorities, after being instructed by the Company to cooperate, or the willful destruction or failure to preserve documents or other materials known to be relevant to such investigation or the inducement of others to fail to cooperate or to produce documents or other materials in connection with such investigation; provided, however, the actions or conduct described in clauses (iv) and (v) above shall only constitute Cause if the Company provides the Executive with written notice thereof and the Executive has not, within 30 days of receipt such written notice, discontinued the cited conduct or remedied the failure to perform and further provided that lawful actions taken by the Executive in the exercise of his rights under the United States Constitution shall not constitute a breach of subsection (vi) above.

(ii) Good Reason. For purposes of this Agreement, "Good Reason" shall mean that the Executive has complied with the "Good Reason Process" (hereinafter defined) following the occurrence of any of the following events: (i) a material diminution in the Executive's responsibilities, authority and function, an adverse change to Executive's job title, or a change in Executive's reporting relationship that results in the Executive no longer reporting directly to the CEO; (ii) a material reduction in Base Salary except pursuant to a salary reduction program affecting substantially all of the employees of the Company, provided that it does not adversely affect the Executive to a greater extent than other similarly situated employees; (iii) a material change in the principal geographic location at which the Executive provides services to the Company outside of the Greater Boston, Massachusetts area; or (iv) the material breach of this Agreement by the Company (each a "Good Reason Condition"). Good Reason Process shall mean that (i) the Executive reasonably determines in good faith that a Good Reason Condition has occurred; (ii) the Executive notifies the Company in writing of the first occurrence of the Good Reason Condition within 60 days of the occurrence of such condition; (iii) the Executive cooperates in good faith with the Company's efforts, for a period not less than 30 days following such notice (the "Cure Period"), to remedy the Good Reason Condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) the Executive terminates employment within 60 days after the end of the Cure Period. If the Company cures the Good Reason Condition during the Cure Period, Good Reason shall be deemed not to have occurred.

(iii) Notice of Termination. Except for termination as specified in Section 3(c), any termination of the Executive's employment by either the Company or the Executive shall be communicated by written Notice of Termination to the other party hereto. For purposes of this Agreement, a "Notice of Termination" shall mean a notice which shall indicate the specific termination provision in this Agreement relied upon.

(iv) Date of Termination. For purposes of this Agreement, "Date of Termination" shall mean: (i) if the Executive's employment is terminated by death, the date of death; (ii) if the Executive's employment is terminated on account of disability under Section 3(d) or by the Company for Cause under Section 3(e), the date on which Notice of Termination is given; (iii) if the Executive's employment terminates as a result of an Involuntary Departure under Section 3(b), the last day of the Notice Period; (iv) if the Executive's employment is terminated by the Executive under Section 3(f) without Good Reason, 30 days after the date on which a Notice of Termination is given (unless the Company waives all or part of the thirty (30) day period).

4. Compensation Upon Termination. If the Executive's employment with the Company is terminated for any reason, the Company shall pay or provide to the Executive (or to the Executive's authorized representative or estate) (i) any Base Salary earned through the Date of Termination; (ii) unpaid expense reimbursements (subject to, and in accordance with Section 2(d) of this Agreement); (iii) subject to Section 3(b)(ii)(D), unused vacation that accrued through the Date of Termination; and (iv) any vested benefits the Executive may have under any employee benefit plan of the Company through the Date of Termination, which vested benefits shall be paid and/or provided in accordance with the terms of such employee benefit plans (together, the "Accrued Benefit") on or before the time required by law but in no event more than 30 days after the Executive's Date of Termination.

5. Change in Control.

(a) Acceleration of Vesting. In the event a Notice of Termination of an Involuntary Termination occurs during the CIC Period, and subject to the Executive signing, within 60 days following the Notice of Termination, a Release and the Release becoming effective and non-revocable within such 60-day period, all time based stock options and time based stock-based awards held by the Executive as of the date of the Notice of Termination, shall vest and become exercisable or nonforfeitable. Notwithstanding the foregoing, if, at the time of a Change in Control, the Company determines in its sole discretion, in reliance upon an opinion of counsel in form and substance satisfactory to the Company, that the acceleration in the prior sentence would not be permissible under applicable law, then in lieu of the acceleration in the prior sentence, all time based stock options and time based stock-based awards held by the Executive as of the date of such Change in Control, shall vest and become exercisable or nonforfeitable as of the date of such Change in Control.

(b) Excise Tax.

(i) Anything in this Agreement to the contrary notwithstanding, in the event that any compensation, payment or distribution by the Company to or for the benefit of the Executive, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise (the "Parachute Payments"), would be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), the following provisions shall apply:

(A) If the Parachute Payments, reduced by the sum of (1) the Excise Tax and (2) the total of the Federal, state, and local income and employment taxes payable by the Executive on the amount of the Parachute Payments which are in excess of the Threshold Amount, are greater than or equal to the Threshold Amount, the Executive shall be entitled to the full benefits payable under this Agreement.

(B) If the Threshold Amount is less than (x) the Parachute Payments, but greater than (y) the Parachute Payments reduced by the sum of (1) the Excise Tax and (2) the total of the Federal, state, and local income and employment taxes on the amount of the Parachute Payments which are in excess of the Threshold Amount, then the Parachute Payments shall be reduced (but not below zero) to the extent necessary so that the sum of all Parachute Payments shall not exceed the Threshold Amount. In such event, the Parachute Payments shall be reduced in the following order: (1) cash payments not subject to Section 409A of the Code; (2) cash payments subject to Section 409A of the Code; (3) equity-based payments and acceleration; and (4) non-cash forms of benefits. To the extent any payment is to be made over time *(e.g.,* in installments, etc.), then the payments shall be reduced in reverse chronological order.

(ii) For the purposes of this Section 5(c), "Threshold Amount" shall mean three times the Executive's "base amount" within the meaning of Section 280G(b)(3) of the Code and the regulations promulgated thereunder less one dollar ($1.00); and "Excise Tax" shall mean the excise tax imposed by Section 4999 of the Code, and any interest or penalties incurred by the Executive with respect to such excise tax.

(iii) All calculations and determinations under Sections 5(c)(i) and 5(c)(ii) shall be made by an independent accounting firm or independent tax counsel appointed by the Company (the "Tax Counsel") whose determinations shall be conclusive and binding on the Company and the Executive for all purposes. For purposes of making the calculations and determinations required by Sections 5(c)(i) and 5(c)(ii), the Tax Counsel may rely on reasonable, good faith assumptions and approximations concerning the application of Section 280G and Section 4999 of the Code. The Company and the Executive shall furnish the Tax Counsel with such information and documents as the Tax Counsel may reasonably request in order to make its determinations under Sections 5(c)(i) and 5(c)(ii). The Company shall bear all costs the Tax Counsel may reasonably incur in connection with its services.

(c) Definitions. For purposes of this Section 5, "Change in Control" shall mean any of the following:

(i) any "person," as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended (the "Act") (other than Parent, any of its subsidiaries, or any trustee, fiduciary or other person or entity holding securities under any employee benefit plan or trust of Parent or any of its subsidiaries), together with all "affiliates" and "associates" (as such terms are defined in Rule 12b-2 under the Act) of such person, shall become the "beneficial owner" (as such term is defined in Rule 13d-3 under the Act), directly or indirectly, of securities of Parent representing 50 percent or more of the combined voting power of the Company's then outstanding securities having the right to vote in an election of the Board ("Voting Securities") (in such case other than as a result of an acquisition of securities directly from Parent); or

(ii) the date a majority of the members of the Board is replaced during any 12-month period by directors whose appointment or election is not endorsed by a majority of the members of the Board before the date of the appointment or election; or

(iii) the consummation of (A) any consolidation or merger of Parent where the stockholders of Parent, immediately prior to the consolidation or merger, would not, immediately after the consolidation or merger, beneficially own (as such term is defined in Rule 13d-3 under the Act), directly or indirectly, shares representing in the aggregate more than 50 percent of the voting shares of the company issuing cash or securities in the consolidation or merger (or of its ultimate parent corporation, if any), or (B) any sale or other transfer (in one transaction or a series of transactions contemplated or arranged by any party as a single plan) of all or substantially all of the assets of Parent.

Notwithstanding the foregoing, a "Change in Control" shall not be deemed to have occurred for purposes of the foregoing clause (i) solely as the result of an acquisition of securities by Parent which, by reducing the number of shares of Voting Securities outstanding, increases the proportionate number of Voting Securities beneficially owned by any person to 50 percent or more of the combined voting power of all of the then outstanding Voting Securities; provided, however, that if any person referred to in this sentence shall thereafter become the beneficial owner of any additional shares of Voting Securities (other than pursuant to a stock split, stock dividend, or similar transaction or as a result of an acquisition of securities directly from Parent) and immediately thereafter beneficially owns 50 percent or more of the combined voting power of all of the then outstanding Voting Securities, then a "Change in Control" shall be deemed to have occurred for purposes of the foregoing clause (i). For the avoidance of doubt, a migratory merger of Parent for the principal purpose of redomiciling Parent shall not constitute a Change in Control.

6. Section 409A.

(a) Anything in this Agreement to the contrary notwithstanding, if at the time of the Executive's separation from service within the meaning of Section 409A of the Code, the Company determines that the Executive is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that the

Executive becomes entitled to under this Agreement on account of the Executive's separation from service would be considered deferred compensation subject to the 20 percent additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) six months and one day after the Executive's separation from service, or (B) the Executive's death. If any such delayed cash payment is otherwise payable on an installment basis, the first payment shall include a catch-up payment covering amounts that would otherwise have been paid during the six-month period but for the application of this provision, and the balance of the installments shall be payable in accordance with their original schedule. Solely for purposes of Section 409A of the Code, each installment payment under this Agreement is considered a separate payment.

(b) All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by the Executive during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year. Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

(c) To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon the Executive's termination of employment, then such payments or benefits shall be payable only upon the Executive's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h).

(d) The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. The parties agree that this Agreement may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party.

(e) The Company makes no representation or warranty and shall have no liability to the Executive or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

7. Proprietary Information, Noncompetition and Cooperation.

(a) Restrictive Covenants and Assignment of Inventions. The Executive has entered into the Proprietary Information and Inventions Agreement (the "Confidentiality and Assignment Agreement"), attached hereto as Exhibit A, and agrees to continue to honor the obligations and restrictive covenants set forth in the Confidentiality and Assignment Agreement, the terms of which are incorporated by reference as material terms of this Agreement.

(b) Non-Competition and Non-Solicitation. In order to protect the Company's proprietary information and good will, during the Executive's employment with the Company and for a period of twelve (12) months following the (i) the delivery of a Notice of Termination, in the case of an Involuntary Departure or (ii) the termination of the Executive's employment for any other reason (the "Restricted Period"), the Executive will not directly or indirectly, whether as owner, partner, shareholder, director, manager, consultant, agent, employee, co-venturer or otherwise, engage, participate or invest in any Competing Business. For purposes hereof, the term "Competing Business" shall mean any entity engaged in the discovery, development or commercialization of CAS9 technology for human therapeutics. Notwithstanding the foregoing, nothing contained hereinabove or hereinbelow shall be deemed to prohibit the Executive from (i) acquiring, solely as an investment, shares of capital stock (or other interests) of any corporation (or other entity) not exceeding 2% of such corporation's (or other entity's) then outstanding shares of capital stock (or equity interest), or (ii) working for a line of business, division or unit of a larger entity that competes with the Company as long as the Executive's activities for such line of business, division or unit do not involve work by the Executive on matters that are directly competitive with the Company's business. In addition, during the Restricted Period, the Executive will not, directly or indirectly, in any manner, other than for the benefit of the Company (i) divert or take away customers of the Company or any of its suppliers; and/or (ii) solicit, entice, attempt to persuade any other employee or consultant of the Company to leave the Company for any reason (other than the termination of subordinate employees undertaken in the course of the Executive's employment with the Company). The Executive acknowledges and agrees that if the Executive violates any of the provisions of this paragraph 7(b), the running of the Restricted Period will be extended by the time during which the Executive engages in such violation(s).

(c) Litigation and Regulatory Cooperation. During and after the Executive's employment, the Executive shall use reasonable efforts to cooperate with the Company in the defense or prosecution of any claims or actions now in existence or that may be brought in the future against or on behalf of the Company that relate to events or occurrences that transpired while the Executive was employed by the Company. The Executive's cooperation in connection with such claims or actions shall include, but not be limited to, being available to meet with counsel to prepare for discovery or trial and to act as a witness on behalf of the Company at mutually convenient times. During and after the Executive's employment, the Executive shall use reasonable efforts to cooperate with the Company in connection with any investigation or review of any federal, state or local regulatory authority as any such investigation or review relates to events or occurrences that transpired while the Executive was employed by the Company. The Company shall reimburse the Executive for any reasonable out-of-pocket expenses incurred in connection with the Executive's performance of obligations pursuant to this Section 7(c).

(d) Injunction. The Executive agrees that it would be difficult to measure any damages caused to the Company that might result from any breach by the Executive of the promises set forth in this Section 7 and the Confidentiality and Assignment Agreement, and that in any event money damages would be an inadequate remedy for any such breach. Accordingly, subject to Section 8 of this Agreement, the Executive agrees that if the Executive breaches, or proposes to breach, any portion of this Agreement and the Confidentiality and Assignment Agreement, the Company shall be entitled, in addition to all other remedies that it may have, to an injunction or other appropriate equitable relief to restrain any such breach without showing or proving any actual damage to the Company.

(e) Protected Reporting; Defend Trade Secrets Act Immunity. Nothing in this Agreement or the Confidentiality and Assignment Agreement, and nothing in any policy or procedure, in any other confidentiality, employment, separation agreement or in any other document or communication from the Company limits the Executive's ability to file a charge or complaint with any government agency concerning any acts or omissions that the Executive may believe constitute a possible violation of federal or state law or making other disclosures that are protected under the whistleblower provisions of applicable federal or state law regulation or affects the Executive's ability to communicate with any government agency or otherwise participate in any investigation or proceeding that may be conducted by a government agency, including by providing documents or other information, without notice to the Company. In addition, for the avoidance of doubt, pursuant to the federal Defend Trade Secrets Act of 2016, the Executive shall not be held criminally or civilly liable under any federal or state trade secret law for the disclosure of a trade secret that (i) is made (A) in confidence to a federal, state, or local government official, either directly or indirectly, or to an attorney; and (B) solely for the purpose of reporting or investigating a suspected violation of law; or (ii) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal.

8. Arbitration of Disputes. Any controversy or claim arising out of or relating to this Agreement or the breach thereof or otherwise arising out of the Executive's employment or the termination of that employment (including, without limitation, any claims of unlawful employment discrimination whether based on age or otherwise) shall, to the fullest extent permitted by law, be settled by arbitration in any forum and form agreed upon by the parties or, in the absence of such an agreement, under the auspices of the American Arbitration Association ("AAA") in Boston, Massachusetts in accordance with the Employment Arbitration Rules of the AAA, including, but not limited to, the rules and procedures applicable to the selection of arbitrators. In the event that any person or entity other than the Executive or the Company may be a party with regard to any such controversy or claim, such controversy or claim shall be submitted to arbitration subject to such other person or entity's agreement. Judgment upon the award rendered by the arbitrator may be entered in any court having jurisdiction thereof. This Section 8 shall be specifically enforceable. Notwithstanding the foregoing, this Section 8 shall not preclude either party from pursuing a court action for the sole purpose of obtaining a temporary restraining order or a preliminary injunction in circumstances in which such relief is appropriate; provided that any other relief shall be pursued through an arbitration proceeding pursuant to this Section 8.

9. Consent to Jurisdiction. To the extent that any court action is permitted consistent with or to enforce Section 8 of this Agreement, the parties hereby agree that the Middlesex County Superior Court of The Commonwealth of Massachusetts shall have exclusive jurisdiction of such dispute. Accordingly, with respect to any such court action, the Executive submits to the personal jurisdiction of such courts.

10. Integration. This Agreement and the Confidentiality and Assignment Agreement constitutes the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior agreements between the Parties concerning such subject matter.

11. Withholding. All payments made by the Company to the Executive under this Agreement shall be net of any tax or other amounts required to be withheld by the Company under applicable law.

12. Successor to the Executive. This Agreement shall inure to the benefit of and be enforceable by the Executive's personal representatives, executors, administrators, heirs, distributees, devisees and legatees. In the event of the Executive's death after her termination of employment but prior to the completion by the Company of all payments due him under this Agreement, the Company shall continue such payments to the Executive's beneficiary designated in writing to the Company prior to her death (or to her estate, if the Executive fails to make such designation).

13. Enforceability. If any portion or provision of this Agreement (including, without limitation, any portion or provision of any section of this Agreement) shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

14. Survival. The provisions of this Agreement and the Confidentiality and Assignment Agreement shall survive the termination of this Agreement and/or the termination of the Executive's employment to the extent necessary to effectuate the terms contained herein.

15. Waiver. No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of any party to require the performance of any term or obligation of this Agreement, or the waiver by any party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

16. Notices. Any notices, requests, demands and other communications provided for by this Agreement shall be sufficient if in writing and delivered in person or sent by a nationally recognized overnight courier service or by registered or certified mail, postage prepaid, return receipt requested, to the Executive at the last address the Executive has filed in writing with the Company or, in the case of the Company, at its main offices, attention of the CEO and a copy of such notice shall be sent to Crispr AG, Attention: Chief Financial Officer, at the main offices of Crispr AG.

17. Amendment. This Agreement may be amended or modified only by a written instrument signed by the Executive and by a duly authorized representative of the Company.

18. Governing Law. This is a Massachusetts contract and shall be construed under and be governed in all respects by the laws of the Commonwealth of Massachusetts, without giving effect to the conflict of laws principles of such Commonwealth. With respect to any disputes concerning federal law, such disputes shall be determined in accordance with the law as it would be interpreted and applied by the United States Court of Appeals for the First Circuit.

19. Counterparts. This Agreement may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original; but such counterparts shall together constitute one and the same document.

20. Assignment and Transfer by the Company. The Company will have the right to assign and/or transfer this Agreement to its affiliates, successors and assigns. The Executive expressly consents to be bound by the provisions of this Agreement for the benefit of the Company or any parent, subsidiary or affiliate to whose employ the Executive may be transferred without the necessity that this Agreement be re-signed at the time of such transfer.

[Remainder of page intentionally left blank. Signature page follows.]

IN WITNESS WHEREOF, the parties have executed this Agreement effective on the date and year first above written.

CRISPR THERAPEUTICS, INC.

By: /s/ Rodger Novak

EXECUTIVE

/s/ James R. Kasinger

James R. Kasinger

EXHIBIT A

Proprietary Information and Inventions Agreement

EMPLOYMENT AGREEMENT

This Employment Agreement ("Agreement") is made as of the 1st day of August, 2017, between CRISPR Therapeutics, Inc., a Delaware corporation (the "Company"), and Tony W. Ho (the "Executive" and, together with the Company, the "Parties" or each individually, a "Party"),

WHEREAS, the Company is a wholly owned subsidiary of CRISPR Therapeutics AG ("Parent" or "CRISPR AG");

WHEREAS, Parent and the Company are each subject to the Swiss Ordinance act against excessive compensation in listed companies as a result of the of listing of the common shares of Parent on the NASDAQ Global Market;

WHEREAS, the Company and the Executive are parties to that certain Letter Agreement dated July 11,2017 (the "Prior Agreement"), which contemplated an employment agreement in the form hereof.

NOW, THEREFORE, in consideration of the mutual covenants and agreements herein contained and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties agree as follows:

1. Position and Duties. During the period which the Executive is employed pursuant to this Agreement (the "Employment Period"), the Executive shall serve as the Executive Vice President, Head of Research and Development of the Company, and shall have responsibilities and duties consistent with such position and such other responsibilities and duties which are not inconsistent with the Executive's skills and experience or his ability to discharge his responsibilities as Executive Vice President, Head of Research and Development as may from time to time be prescribed by the Chief Executive Officer of the Company (the "CEO"). The Executive shall devote the Executive's full working time and efforts to the business and affairs of the Company except as otherwise permitted under Section 3(b)(i). Notwithstanding the foregoing, the Executive may engage in charitable or other community activities, as long as such services and activities are disclosed to the Board of Directors of Parent (the "Board") and do not materially interfere with the Executive's performance of the Executive's duties to the Company as provided in this Agreement. During the Employment Period, the Executive's principal place of employment will be in the Greater Boston, Massachusetts area; however, the Company may require the Executive to travel temporarily to other locations in connection with the Company's business.

2. Compensation and Related Matters.

(a) Base Salary. During the Employment Period, the Company shall pay the Executive, as compensation for the performance of the Executive's duties and obligations under this Agreement, an annual base salary of $410,000, payable in a manner that is consistent with the Company's usual payroll practices for senior executives. The Executive's Base Salary shall be reviewed annually by the Board or the Compensation Committee of the Board or any successor to such committee (the "Committee") for adjustment. Such adjustment, if any, shall be within the sole discretion of the Board or, to the extent delegated by the Board, the Committee. The annual base salary in effect at any given time is referred to herein as "Base Salary." The Base Salary shall not be reduced at any time without the express written consent of the Executive.

(b) Annual Bonus. During the Employment Period, the Executive shall be eligible to receive an annual target bonus (a "Bonus"-) if, as reasonably determined by the Board or, to the extent delegated by the Board, the Committee one or more of the performance targets annually determined by the Board or the Committee ("Performance Targets") is achieved. If all of the Performance Targets are achieved, the Bonus will equal not less than 45 percent of the Executive's Base Salary (the "Target Bonus"). In the event that less than all of the Performance Targets are met by Executive, the Bonus paid in respect of this paragraph may be less than the Target Bonus. Except as set forth in Section 4 hereof, the Executive must be employed by the Company on the final day of the year with respect to which any such Bonus is earned, and any such Bonus shall be paid not later than *2V2* months after the end of such calendar year. The Executive's target bonus opportunity as a percentage of Base Salary may be reviewed periodically and adjusted in the sole discretion of the Board or, to the extent delegated by the Board, the Committee. After any such adjustment, the term "Target Bonus" shall refer to the increased amount. The Target Bonus shall not be reduced at any time without the express prior written consent of the Executive.

(c) Equity Compensation. The Executive shall be eligible to participate in Parent's equity incentive plan according to its terms and conditions, as defined by Parent from time to time in its sole discretion. Both entitlement to any equity awards and the amount shall be determined by Parent in its sole discretion.

(d) Expenses. During the Employment Period, the Executive shall be entitled to receive reimbursement for all reasonable expenses incurred by him in performing services hereunder, in accordance with the policies and procedures then in effect and established by the Company for its senior executive officers.

(e) Other Benefits. During the Employment Period, the Executive shall be entitled to participate in or receive benefits under any employee benefit plan or arrangement currently maintained or which may, in the future, be made available by the Company generally to its executives and key management employees, subject to and on a basis consistent with the terms, conditions and overall administration of such plan or arrangement. Any payments or benefits payable to the Executive under a plan or arrangement referred to in this Section 2(e) in respect of any calendar year during which the Executive is employed by the Company for less than the whole of such year shall, unless otherwise provided in the applicable plan or arrangement, be prorated in accordance with the number of days in such calendar year during which the Executive is so employed. Should any such payments or benefits accrue on a fiscal (rather than calendar) year, then the proration in the preceding sentence shall be on the basis of a fiscal year rather than calendar year.

(f) Vacations. The Executive shall be entitled to accrue up to 20 paid vacation days in each year, which shall be accrued ratably. In other respects, the Company's vacation policy as the same may then be in effect shall apply to vacations.

(g) Approval by Shareholders' Meeting and Mandatory Law. Any compensation (including bonus, equity awards and fringe benefits) to be paid under this Agreement, is, to the extent required by Swiss laws and the Parent's Article of Association, subject to approval by the general meeting of shareholders' of Parent. In the event of a conflict between the Agreement and applicable mandatory Swiss law, the Company shall have the right to unilaterally modify the Agreement to the extent necessary to comply with mandatory law with immediate effect.

3. Termination.

(a) General. The Executive's employment shall continue until it is terminated in accordance with this Agreement. Upon service of a Notice of Termination (as defined below), the Executive shall resign from all offices and functions assumed in relation to this Agreement effective upon first request of the Company but shall remain entitled to receive the payments and benefits described in Sections 3(b), 4 and 5(a), to the extent applicable.

(b) Termination by the Company without Cause or by Executive for Good Reason; Notice Period. In the event that the Company elects to terminate the Executive's employment without Cause (as defined below) or the Executive elects to resign from Executive's employment with Good Reason (as defined below) (in either case an "Involuntary Departure"), the Party electing to end the employment relationship shall provide the other Party with a Notice of Termination (as defined below) of the Involuntary Departure specifying a notice period (the "Notice Period") of six (6) months, effective as per the end of a calendar month; provided that, in the case that the Notice of Termination of an Involuntary Departure is provided within the 12 month period following a Change in Control (the "Change in Control Period" or "CIC Period"), then the Notice Period shall be 12 months.

(i) During the Notice Period following a Notice of Termination of an Involuntary Departure, the Executive shall continue to be available to provide services to the extent requested by the Company or the Board, provided at any time during the Notice Period the Company may replace the Executive's position and/or direct the Executive to perform other or reduced work; provided further that, upon the 15th day following such Notice of Termination (or such earlier date as the Company shall determine in its sole discretion), the Company shall release the Executive from his working obligations pursuant to Section 3(b)(i) (except to the extent the parties otherwise agree) and place the Executive on garden leave for the remainder of the Notice Period ("Garden Leave"). During such Garden Leave, the Executive (A) may enter into consulting arrangements and accept board positions provided such outside business activities do not violate Executive's obligations under Section 7 and (B) shall be free to engage in other employment provided that such employment does not violate Executive's obligations under Section 7. The Company shall be prohibited during the Notice Period from reducing any compensation to which the Executive is entitled to receive during the Notice Period pursuant to Section 3(b)(ii).

(ii) With respect to compensation during the Notice Period following a Notice of Termination of an Involuntary Departure, and subject to (i) the Executive signing, within 30 days following the date that the Notice of Termination is given, a

Release of Claims in a form reasonably required by the Company (the "Release") and (ii) Section 6, the Executive: (A) shall continue to receive the Base Salary (without regard to any reduction in Base Salary that would provide a basis for Executive's Good Reason resignation) and employee benefits consistent with the Company's then existing benefits plans and programs at the same costs as such benefits are provided to similarly situated active employees;; (B) shall be entitled to receive an amount equal to the Target Bonus (without regard to any reduction in Target Bonus that would provide a basis for Executive's Good Reason resignation) with respect to the Notice Period (i.e., a prorated Target Bonus based upon the number of days in the applicable Notice Period), which prorated Target Bonus amount shall be payable in a lump sum no more than 60 days after the Notice of Termination (provided that if the 60-day period begins in one calendar year and ends in a second calendar year, such Target Bonus shall be paid in the second calendar year); (C) shall continue to vest through the last day of the Notice Period in any equity awards outstanding as of the date the Notice of Termination is given; provided, and notwithstanding the foregoing, Section 5(a) may apply if the Notice of Termination of an Involuntary Departure occurs during a CIC Period and (D) shall not continue to accrue vacation under Section 2(f).

(iii) If during the Notice Period following a Notice of Termination of an Involuntary Departure, the Executive breaches any of the material provisions contained in Section 7(b) of this Agreement or the material obligations in the Confidentiality and Assignment Agreement, then the Company shall provide a restated Notice of Termination and the Notice Period shall end on the earlier date set forth in the restated Notice of Termination (provided that such date shall be no earlier than the date upon which the restated Notice of Termination is delivered).

(c) Death. The Executive's employment hereunder shall terminate upon his death.

(d) Disability. The Company may terminate the Executive's employment if the Executive is disabled and unable to perform the essential functions of the Executive's then existing position or positions with or without reasonable accommodation for a period of 180 days (which need not be consecutive) in any 12-month period, provided that, if the Company maintains a long-term disability plan for the Company's employees at the time of such termination, the Executive's disability would, if the Executive otherwise qualified for disability benefits under such long-term disability plan, result in the Executive receiving benefits coverage for the longest period of time provided under such long-term disability plan. If any question shall arise as to whether during any period the Executive is disabled so as to be unable to perform the essential functions of the Executive's then existing position or positions with or without reasonable accommodation, the Executive may, and at the request of the Company shall, submit to the Company a certification in reasonable detail by a physician mutually acceptable to Executive and Company as to whether the Executive is so disabled or how long such disability is expected to continue, and such certification shall for the purposes of this Agreement be conclusive of the issue. If the Executive and the Company cannot agree as to a qualified physician, each shall appoint such a physician and those two physicians shall select a third who shall make such determination in writing. The determination of disability made in writing to the Company and the Executive shall be final and conclusive for all purposes of this Agreement.

The Executive shall cooperate with any reasonable request of the physician in connection with such certification. Nothing in this Section 3(d) shall be construed to waive the Executive's rights, if any, under existing law including, without limitation, the Family and Medical Leave Act of 1993,29 U.S.C. §2601 *et seq.* and the Americans with Disabilities Act, 42 U.S.C. §12101 *et seq.*

(e) Termination by Company for Cause. The Company may terminate the Executive's employment hereunder for Cause.

(f) Termination by the Executive Without Good Reason. The Executive may terminate his employment hereunder at any time without Good Reason.

(g) Definitions:

(i) Cause. For purposes of this Agreement, "Cause" shall mean: (i)conduct by the Executive constituting a material act of misconduct in connection with the performance of the Executive's duties that results in material harm to the Company, including, without limitation, misappropriation of funds or property of the Company or any of its subsidiaries or affiliates other than the occasional, customary and de minimis use of Company property for personal purposes; (ii) the Executive's indictment for, conviction of or plea of guilty or nolo contendre to (A) any felony; or (B) a misdemeanor involving moral turpitude, deceit, dishonesty or fraud; (iii) continued non-performance by the Executive of the Executive's material responsibilities hereunder (other than by reason of the Executive's physical or mental illness, incapacity or disability) which has continued for more than 30 days following written notice of such non-performance from the CEO; (iv) a material breach by the Executive of any of the material provisions contained in Section 7 of this Agreement or the material obligations arising pursuant to the Confidentiality and Assignment Agreement (as hereinafter defined); (v) a material violation by the Executive of any of the Company's written employment policies, which if possible to cure is not cured within 30 days following written notice of such violation; or (vi) failure to cooperate with a bona fide internal investigation or an investigation by regulatory or law enforcement authorities, after being instructed by the Company to cooperate, or the willful destruction or failure to preserve documents or other materials known to be relevant to such investigation or the inducement of others to fail to cooperate or to produce documents or other materials in connection with such investigation; provided that the exercise by Executive of his rights under the United States Constitution shall not constitute a breach of this subsection (vi).

(ii) Good Reason. For purposes of this Agreement, "Good Reason" shall mean that the Executive has complied with the "Good Reason Process" (hereinafter defined) following the occurrence of any of the following events: (i) a material diminution in the Executive's responsibilities, authority or duties; (ii) a material reduction in Base Salary or Target Bonus which has not been consented to by the Executive; (iii) a material change in the principal geographic location at which the Executive provides services to the Company outside of the Greater Boston, Massachusetts area; or (iv) the material breach of this Agreement by the Company (each a "Good Reason Condition"). Good Reason Process shall mean that (i) the Executive reasonably determines in good faith that a Good Reason Condition has occurred; (ii) the Executive notifies the Company in writing of the occurrence of the Good Reason Condition within 90 days of the occurrence of such condition; (iii) the Executive cooperates in good faith with the Company's efforts, for a period not less than 30 days following such notice (the "Cure Period"), to remedy the Good Reason Condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) the Executive terminates employment within 60 days after the end of the Cure Period. If the Company cures the Good Reason Condition during the Cure Period, Good Reason shall be deemed not to have occurred.

(iii) Notice of Termination. Except for termination as specified in Section 3(c), any termination of the Executive's employment by either the Company or the Executive shall be communicated by written Notice of Termination to the other party hereto. For purposes of this Agreement, a "Notice of Termination" shall mean a notice which shall indicate the specific termination provision in this Agreement relied upon.

(iv) Date of Termination. For purposes of this Agreement, "Date of Termination" shall mean: (i) if the Executive's employment is terminated by death, the date of death; (ii) if the Executive's employment is terminated on account of disability under Section 3(d) or by the Company for Cause under Section 3(e), the date on which Notice of Termination is given; (iii) if the Executive's employment terminates as a result of an Involuntary Departure under Section 3(b), the last day of the Notice Period; (iv) if the Executive's employment is terminated by the Executive under Section 3(f) without Good Reason, 30 days after the date on which a Notice of Termination is given (unless the Company waives all or part of the thirty (30) day period).

4. Compensation Upon Termination. If the Executive's employment with the Company is terminated for any reason, the Company shall pay or provide to the Executive (or to the Executive's authorized representative or estate) (i) any Base Salary earned through the Date of Termination; (ii) unpaid expense reimbursements (subject to, and in accordance with Section 2(d) of this Agreement); (iii) subject to Section 3(b)(ii)(D), unused vacation that accrued through the Date of Termination; (iv) except in the case the Executive's employment is terminated by the Company for Cause under Section 3(e), any unpaid Bonus earned for the year prior to the year in which the Notice of Termination is delivered; (v) a prorated portion of the Bonus the Executive would have earned for the year in which the Notice of Termination is delivered, based on actual performance as determined in good faith by the Board or the Committee (with such proration based on the portion of such year elapsed prior to delivery of the Notice of Termination); and (vi) any vested benefits the Executive may have under any employee benefit plan of the Company through the Date of Termination, which vested benefits shall be paid and/or provided in accordance with the terms of such employee benefit plans (together, the "Accrued Benefit") on or before the time required by law but in no event more than 30 days after the Executive's Date of Termination, provided that the amounts payable under clauses (iv) and (v), if any, shall be paid at the same time Bonuses for the given year are paid to the Company's executive employees generally.

5. Change in Control.

(a) Acceleration of Vesting. In the event a Notice of Termination of an Involuntary Termination occurs during the CIC Period or within two months prior to a Change in Control, or in the event the Executive delivers a Notice of Termination for any reason not sooner than 6 months after the occurrence of a Change in Control, and subject to the Executive signing, within 60 days following the Notice of Termination, a Release and the Release becoming effective and non-revocable within such 60-day period, all stock options and stock-based awards held by the Executive as of the date of the Notice of Termination, shall vest and become exercisable or nonforfeitable. Notwithstanding the foregoing, if, at the time of a Change in Control, the Company determines in its sole discretion, in reliance upon an opinion of counsel in form and substance satisfactory to the Company, that the acceleration in the prior sentence would not be permissible under applicable law, then in lieu of the acceleration in the prior sentence, all stock options and stock-based awards held by the Executive as of the date of such Change in Control, shall vest and become exercisable or nonforfeitable as of the date of such Change in Control.

(b) Excise Tax.

(i) Anything in this Agreement to the contrary notwithstanding, in the event that any compensation, payment or distribution by the Company to or for the benefit of the Executive, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise, in each case, that are treated as contingent on a "change in ownership of control" within the meaning of Treasury Regulations Section 1.280G-1 (the "Parachute Payments"), would be subject to the excise tax imposed by Section 4999 of the Code (including any interest or penalties incurred by the Executive with respect to such excise tax, the "Excise Tax"), the following provisions shall apply:

(A) If the Parachute Payments, reduced by the sum of (1) the Excise Tax and (2) the total of the Federal, state, and local income and employment taxes (for the avoidance of doubt, without duplication of the Excise Tax) payable by the Executive on the amount of the Parachute Payments which are in excess of the Threshold Amount, are greater than or equal to the Threshold Amount, the Executive shall be entitled to the full benefits payable under this Agreement.

(B) If the Threshold Amount is less than (x) the Parachute Payments, but greater than (y) the Parachute Payments reduced by the sum of (1) the Excise Tax and (2) the total of the Federal, state, and local income and employment taxes on the amount of the Parachute Payments which are in excess of the Threshold Amount, then the Parachute Payments shall be reduced (but not below zero) to the minimum extent necessary so that the sum of all Parachute Payments shall not exceed the Threshold Amount. In such event, the Parachute Payments shall be reduced in the following order: (1) cash severance payments not subject to Section 409A of the Code; (2) non-cash severance payments other than equity acceleration that are exempt from Section 409A of the Code; (3) other cash or non-cash payments that are exempt from Section 409A; and (4) other payments or benefits (reduced in a manner that complies with Section 409A of the Code). To the extent any payment is to be made over time *(e.g.,* in installments, etc.), then the payments shall be reduced in reverse chronological order.

(ii) For the purposes of this Section 5(c), "Threshold Amount" shall mean three times the Executive's "base amount" within the meaning of Section 280G(b)(3) of the Code and the regulations promulgated thereunder less one dollar ($1.00).

(iii) All calculations and determinations under Sections 5(c)(i) and 5(c)(ii) shall be made by an independent accounting firm or independent tax counsel appointed by the Company (the "Tax Counsel") whose determinations shall be conclusive and binding on the Company and the Executive for all purposes. For purposes of making the calculations and determinations required by Sections 5(c)(i) and 5(c)(ii), the Tax Counsel may rely on reasonable, good faith assumptions and approximations concerning the application of Section 280G and Section 4999 of the Code. The Company and the Executive shall furnish the Tax Counsel with such information and documents as the Tax Counsel may reasonably request in order to make its determinations under Sections 5(c)(i) and 5(c)(ii). The Company shall bear all costs the Tax Counsel may reasonably incur in connection with its services.

(c) Definitions. For purposes of this Section 5, "Change in Control" shall mean any of the following:

(i) any "person," as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended (the "Act") (other than Parent, any of its subsidiaries, or any trustee, fiduciary or other person or entity holding securities under any employee benefit plan or trust of Parent or any of its subsidiaries), together with all "affiliates" and "associates" (as such terms are defined in Rule 12b-2 under the Act) of such person, shall become the "beneficial owner" (as such term is defined in Rule 13d-3 under the Act), directly or indirectly, of securities of Parent representing 50 percent or more of the combined voting power of the Company's then outstanding securities having the right to vote in an election of the Board ("Voting Securities") (in such case other than as a result of an acquisition of securities directly from Parent); or

(ii) the date a majority of the members of the Board is replaced during any 12-month period by directors whose appointment or election is not endorsed by a majority of the members of the Board before the date of the appointment or election; or

(iii) the consummation of (A) any consolidation or merger of Parent where the stockholders of Parent, immediately prior to the consolidation or merger, would not, immediately after the consolidation or merger, beneficially own (as such term is defined in Rule 13d-3 under the Act), directly or indirectly, shares representing in the aggregate more than 50 percent of the voting shares of the company issuing cash or securities in the consolidation or merger (or of its ultimate parent corporation, if any), or (B) any sale or other transfer (in one transaction or a series of transactions contemplated or arranged by any party as a single plan) of all or substantially all of the assets of Parent.

Notwithstanding the foregoing, a "Change in Control" shall not be deemed to have occurred for purposes of the foregoing clause (i) solely as the result of an acquisition of securities by Parent which, by reducing the number of shares of Voting Securities outstanding, increases the proportionate number of Voting Securities beneficially owned by any person to 50 percent or more of the combined voting power of all of the then outstanding Voting Securities; provided, however, that if any person referred to in this sentence shall thereafter become the beneficial owner of any additional shares of Voting Securities (other than pursuant to a stock split, stock dividend, or similar transaction or as a result of an acquisition of securities directly from Parent) and immediately thereafter beneficially owns 50 percent or more of the combined voting power of all of the then outstanding Voting Securities, then a "Change in Control" shall be deemed to have occurred for purposes of the foregoing clause (i). For the avoidance of doubt, a migratory merger of Parent for the principal purpose of redomiciling Parent shall not constitute a Change in Control.

6. <u>Section 409A.</u>

(a) Anything in this Agreement to the contrary notwithstanding, if at the time of the Executive's separation from service within the meaning of Section 409A of the Code, the Company determines that the Executive is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that the Executive becomes entitled to under this Agreement on account of the Executive's separation from service would be considered deferred compensation subject to the 20 percent additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) six months and one day after the Executive's separation from service, or (B) the Executive's death. If any such delayed cash payment is otherwise payable on an installment basis, the first payment shall include a catch-up payment covering amounts that would otherwise have been paid during the six-month period but for the application of this provision, and the balance of the installments shall be payable in accordance with their original schedule. Solely for purposes of Section 409A of the Code, each installment payment under this Agreement is considered a separate payment.

(b) All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by the Executive during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year. Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

(c) To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon the Executive's termination of employment, then such payments or benefits shall be payable only upon the Executive's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h).

(d) The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. The parties agree that this Agreement may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party.

(e) The Company makes no representation or warranty and shall have no liability to the Executive or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

7. Proprietary Information, Noncompetition and Cooperation.

(a) Restrictive Covenants and Assignment of Inventions. On August 1, 2017, the Executive has entered into the Proprietary Information and Inventions Agreement (the "Confidentiality and Assignment Agreement"), attached hereto as Exhibit A, and agrees to continue to honor the obligations and restrictive covenants set forth in the Confidentiality and Assignment Agreement, the terms of which are incorporated by reference as material terms of this Agreement.

(b) Non-Competition and Non-Solicitation. In order to protect the Company's proprietary information and good will, during the Executive's employment with the Company and for a period of nine (9) months following (i) the delivery of a Notice of Termination, in the case of an Involuntary Departure or (ii) the termination of the Executive's employment for any other reason (the "Restricted Period"), the Executive will not directly or indirectly, whether as owner, partner, shareholder, director, manager, consultant, agent, employee, co-venturer or otherwise, engage, participate or invest in any Competing Business. For purposes hereof, the term "Competing Business" shall mean any entity engaged in the discovery, development or commercialization of gene editing technology for human therapeutics. Notwithstanding the foregoing, nothing contained hereinabove or hereinbelow shall be deemed to prohibit the Executive from (i) acquiring, solely as an investment, shares of capital stock (or other interests) of any corporation (or other entity) not exceeding 2% of such corporation's (or other entity's) then outstanding shares of capital stock (or equity interest), or (ii) working for a line of business, division or unit of a larger entity that competes with the Company as long as the Executive's activities for such line of business, division or unit do not involve work by the Executive on matters that are directly competitive with the Company's business. In addition, during the Restricted Period, the Executive will not, directly or indirectly, in any manner, other than for the benefit of the Company (i) divert or take away customers of the Company or any of its suppliers; and/or (ii) solicit, entice, attempt to persuade any other employee or consultant of the Company to leave the Company for any reason (other than the termination of subordinate employees undertaken in the course of my employment with the Company). The Executive acknowledges and agrees that if the Executive violates any of the provisions of this paragraph 7(b), the running of the Restricted Period will be extended by the time during which the Executive engages in such violation(s).

(c) Litigation and Regulatory Cooperation. During and after the Executive's employment, the Executive shall use reasonable efforts to cooperate with the Company in the defense or prosecution of any claims or actions now in existence or that may be brought in the future against or on behalf of the Company that relate to events or occurrences that transpired while the Executive was employed by the Company. The Executive's cooperation in connection with such claims or actions shall include, but not be limited to, being available to meet with counsel to prepare for discovery or trial and to act as a witness on behalf of the Company at mutually convenient times. During and after the Executive's employment, the Executive shall use reasonable efforts to cooperate with the Company in connection with any investigation or review of any federal, state or local regulatory authority as any such investigation or review relates to events or occurrences that transpired while the Executive was employed by the Company. The Company shall reimburse the Executive for any reasonable out-of-pocket expenses incurred in connection with the Executive's performance of obligations pursuant to this Section 7(c).

(d) Injunction. The Executive agrees that it would be difficult to measure any damages caused to the Company that might result from any breach by the Executive of the promises set forth in Section 7(a) and (b) and the Confidentiality and Assignment Agreement, and that in any event money damages would be an inadequate remedy for any such breach. Accordingly, subject to Section 8 of this Agreement, the Executive agrees that if the Executive breaches, or proposes to breach, any portion of this Agreement and the Confidentiality and Assignment Agreement, the Company shall be entitled, in addition to all other remedies that it may have, to an injunction or other appropriate equitable relief to restrain any such breach without showing or proving any actual damage to the Company.

(e) Protected Reporting; Defend Trade Secrets Act Immunity. Nothing in this Agreement or the Confidentiality and Assignment Agreement, and nothing in any policy or procedure, in any other confidentiality, employment, separation agreement or in any other document or communication from the Company limits the Executive's ability to file a charge or complaint with any government agency concerning any acts or omissions that the Executive may believe constitute a possible violation of federal or state law or making other disclosures that are protected under the whistleblower provisions of applicable federal or state law regulation or affects the Executive's ability to communicate with any government agency or otherwise participate in any investigation or proceeding that may be conducted by a government agency, including by providing documents or other information, without notice to the Company. In addition, for the avoidance of doubt, pursuant to the federal Defend Trade Secrets Act of 2016, the Executive shall not be held criminally or civilly liable under any federal or state trade secret law for the disclosure of a trade secret that (i) is made (A) in confidence to a federal, state, or local government official, either directly or indirectly, or to an attorney; and (B) solely for the purpose of reporting or investigating a suspected violation of law; or (ii) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal.

8. Arbitration of Disputes. Any controversy or claim arising out of or relating to this Agreement or the breach thereof or otherwise arising out of the Executive's employment or the termination of that employment (including, without limitation, any claims of unlawful employment discrimination whether based on age or otherwise) shall, to the fullest extent permitted by law, be settled by arbitration in any forum and form agreed upon by the parties or,

in the absence of such an agreement, under the auspices of the American Arbitration Association ("AAA") in Boston, Massachusetts in accordance with the Employment Arbitration Rules of the AAA, including, but not limited to, the rules and procedures applicable to the selection of arbitrators. In the event that any person or entity other than the Executive or the Company may be a party with regard to any such controversy or claim, such controversy or claim shall be submitted to arbitration subject to such other person or entity's agreement. Judgment upon the award rendered by the arbitrator may be entered in any court having jurisdiction thereof. This Section 8 shall be specifically enforceable. Notwithstanding the foregoing, this Section 8 shall not preclude either party from pursuing a court action for the sole purpose of obtaining a temporary restraining order or a preliminary injunction in circumstances in which such relief is appropriate; provided that any other relief shall be pursued through an arbitration proceeding pursuant to this Section 8.

9. Consent to Jurisdiction. To the extent that any court action is permitted consistent with or to enforce Section 8 of this Agreement, the parties hereby agree that the Middlesex County Superior Court of The Commonwealth of Massachusetts shall have jurisdiction of such dispute. Accordingly, with respect to any such court action, the Executive submits to the personal jurisdiction of such courts.

10. Integration. This Agreement and the Confidentiality and Assignment Agreement constitute the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior agreements, including the Prior Agreement (other than Sections __ and __ thereof), between the Parties concerning such subject matter; provided that, the restrictions set forth in Section 4 of the Confidentiality and Assignment Agreement shall not apply following the Restricted Period.

11. Withholding. All payments made by the Company to the Executive under this Agreement shall be net of any tax or other amounts required to be withheld by the Company under applicable law.

12. Successor to the Executive. This Agreement shall inure to the benefit of and be enforceable by the Executive's personal representatives, executors, administrators, heirs, distributees, devisees and legatees. In the event of the Executive's death after his termination of employment but prior to the completion by the Company of all payments due him under this Agreement, the Company shall continue such payments to the Executive's beneficiary designated in writing to the Company prior to his death (or to his estate, if the Executive fails to make such designation).

13. Enforceability. If any portion or provision of this Agreement (including, without limitation, any portion or provision of any section of this Agreement) shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

14. Survival. The provisions of this Agreement and the Confidentiality and Assignment Agreement shall survive the termination of this Agreement and/or the termination of the Executive's employment to the extent necessary to effectuate the terms contained herein.

15. Waiver. No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of any party to require the performance of any term or obligation of this Agreement, or the waiver by any party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

16. Notices. Any notices, requests, demands and other communications provided for by this Agreement shall be sufficient if in writing and delivered in person or sent by a nationally recognized overnight courier service or by registered or certified mail, postage prepaid, return receipt requested, to the Executive at the last address the Executive has filed in writing with the Company or, in the case of the Company, at its main offices, attention of the CEO and a copy of such notice shall be sent to Crispr AG, Attention: Chief Financial Officer, at the main offices of Crispr AG.

17. Amendment. This Agreement may be amended or modified only by a written instrument signed by the Executive and by a duly authorized representative of the Company.

18. Governing Law. This is a Massachusetts contract and shall be construed under and be governed in all respects by the laws of the Commonwealth of Massachusetts, without giving effect to the conflict of laws principles of such Commonwealth. With respect to any disputes concerning federal law, such disputes shall be determined in accordance with the law as it would be interpreted and applied by the United States Court of Appeals for the First Circuit.

19. Counterparts. This Agreement may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original; but such counterparts shall together constitute one and the same document.

20. Assignment and Transfer by the Company. The Company will have the right to assign and/or transfer this Agreement to its affiliates, successors and assigns. The Executive expressly consents to be bound by the provisions of this Agreement for the benefit of the Company or any parent, subsidiary or affiliate to whose employ the Executive may be transferred without the necessity that this Agreement be re-signed at the time of such transfer. The Company shall cause any successor (whether direct or indirect and whether by purchase, merger, consolidation, liquidation or otherwise) to all or substantially all of the Company's business and/or assets to assume the Company's obligations under this Agreement and the Company's failure to cause any such successor to assume such obligations shall constitute a material breach of this Agreement.

21. Attorneys' Fees. The Company will pay on the Executive's behalf the reasonable an documented legal fees incurred by the Executive in connection with the negotiation of this Agreement in an amount not to exceed $5,000.

[Remainder of page intentionally left blank. Signature page follows.]

IN WITNESS WHEREOF, the parties have executed this Agreement effective on the date and year first above written.

CRISPR THERAPEUTICS, INC.

By: /s/ Rodger Novak

EXECUTIVE

/s/ Tony W. Ho

Tony W. Ho

EXHIBIT A

Proprietary Information and Inventions Agreement

Exhibit 10.20

CRISPR THERAPEUTICS AG

2018 STOCK OPTION AND INCENTIVE PLAN

SECTION 1. GENERAL PURPOSE OF THE PLAN; DEFINITIONS

The name of the plan is the CRISPR Therapeutics AG 2018 Stock Option and Incentive Plan (the “Plan”). The purpose of the Plan is to encourage and enable the officers, employees, Non-Employee Directors and Consultants of CRISPR Therapeutics AG (the “Company”) and its Subsidiaries upon whose judgment, initiative and efforts the Company largely depends for the successful conduct of its businesses to acquire a proprietary interest in the Company. It is anticipated that providing such persons with a direct stake in the Company’s welfare will assure a closer identification of their interests with those of the Company and its stockholders, thereby stimulating their efforts on the Company’s behalf and strengthening their desire to remain with the Company.

The following terms shall be defined as set forth below:

“Administrator” means either the Board or the compensation committee of the Board or a similar committee performing the functions of the compensation committee and which is comprised of not less than two Non-Employee Directors who are independent.

“Award” or *“Awards,”* except where referring to a particular category of grant under the Plan, shall include Incentive Stock Options, Non-Qualified Stock Options, Stock Appreciation Rights, Restricted Stock Units, Restricted Stock Awards, Unrestricted Stock Awards and Dividend Equivalent Rights.

“Award Certificate” means a written or electronic document setting forth the terms and provisions applicable to an Award granted under the Plan. Each Award Certificate is subject to the terms and conditions of the Plan.

“Board” means the Board of Directors of the Company.

“Consultant” means any natural person that provides bona fide services to the Company, and such services are not in connection with the offer or sale of securities in a capital-raising transaction and do not directly or indirectly promote or maintain a market for the Company’s securities.

“Covered Employee” means an employee who is a member of the Board of Directors or executive committee and thus subject to approval requirement pursuant to art. 18 of the Swiss Ordinance against excessive compensation in listed stock corporations (*Verordnung gegen übermässige Vergütungen bei börsenkotierten Aktiengesellschaften*).

“*Dividend Equivalent Right*” means an Award entitling the grantee to receive credits based on cash dividends that would have been paid on the shares of Stock specified in the Dividend Equivalent Right (or other award to which it relates) if such shares had been issued to and held by the grantee.

“*Effective Date*” means the date on which the Plan becomes effective as set forth in Section 18.

“*Fair Market Value*” of the Stock on any given date means the fair market value of the Stock determined in good faith by the Administrator; provided, however, that if the Stock is admitted to quotation on the National Association of Securities Dealers Automated Quotation System (“NASDAQ”), NASDAQ Global Market or another national securities exchange, the determination shall be made by reference to market quotations. If there are no market quotations for such date, the determination shall be made by reference to the last date preceding such date for which there are market quotations.

“*Incentive Stock Option*” means any Stock Option designated and qualified as an “incentive stock option” as defined in Section 422 of the US Tax Code.

“*Initial Public Offering*” means the first underwritten, firm commitment public offering pursuant to an effective registration statement under the US Securities Act covering the offer and sale by the Company of its equity securities, or the listing of the shares of the Company at a recognized stock exchange, or such other event as a result of or following which the Stock shall be publicly held.

“*Non-Employee Director*” means a member of the Board who is not also an employee of the Company or any Subsidiary.

“*Non-Qualified Stock Option*” means any Stock Option that is not an Incentive Stock Option.

“*Option*” or “*Stock Option*” means any option to purchase shares of Stock granted pursuant to Section 5.

“*Restricted Shares*” means the shares of Stock underlying a Restricted Stock Award that remain subject to a risk of forfeiture or the Company’s right of repurchase.

“*Restricted Stock Award*” means an Award of Restricted Shares subject to such restrictions and conditions as the Administrator may determine at the time of grant.

“*Restricted Stock Units*” means an Award of stock units subject to such restrictions and conditions as the Administrator may determine at the time of grant.

“*Sale Event*” shall mean (i) the sale of all or substantially all of the assets of the Company on a consolidated basis to an unrelated person or entity, (ii) a merger, reorganization or consolidation pursuant to which the holders of the Company’s outstanding voting power and outstanding stock immediately prior to such transaction do not own a majority of the outstanding voting power and outstanding stock or other equity interests of the resulting or successor entity (or its ultimate parent, if applicable) immediately upon completion of such transaction, (iii) the sale of all of the Stock of the Company to an unrelated person, entity or group thereof acting in concert, or (iv) any other transaction in which the owners of the Company's outstanding voting power immediately prior to such transaction do not own at least a majority of the outstanding voting power of the Company or any successor entity immediately upon completion of the transaction other than as a result of the acquisition of securities directly from the Company.

"*Sale Price*" means the value as determined by the Administrator of the consideration payable, or otherwise to be received by stockholders, per share of Stock pursuant to a Sale Event.

"Section 409A" means Section 409A of the US Tax Code and the regulations and other guidance promulgated thereunder.

"Stock" means the Common Stock, par value CHF 0.03 per share, of the Company, subject to adjustments pursuant to Section 3.

"Stock Appreciation Right" means an Award entitling the recipient to receive shares of Stock (or cash, to the extent explicitly provided for in the applicable Award Certificate) having a value equal to the excess of the Fair Market Value of the Stock on the date of exercise over the exercise price of the Stock Appreciation Right multiplied by the number of shares of Stock with respect to which the Stock Appreciation Right shall have been exercised.

"Subsidiary" means any corporation or other entity (other than the Company) in which the Company has at least a 50 percent interest, either directly or indirectly.

"Ten Percent Owner" means an employee who owns or is deemed to own (by reason of the attribution rules of Section 424(d) of the US Tax Code) more than 10 percent of the combined voting power of all classes of stock of the Company or any parent or subsidiary corporation.

"Unrestricted Stock Award" means an Award of shares of Stock free of any restrictions.

"*US Exchange Act*" means the U.S. Securities Exchange Act of 1934, as amended, and the rules and regulations thereunder.

"*US Securities Act*" means the U.S. Securities Act of 1933, as amended, and the rules and regulations thereunder.

"*US Tax Code*" means the U.S. Internal Revenue Code of 1986, as amended, and any successor Code, and related rules, regulations and interpretations.

SECTION 2. ADMINISTRATION OF PLAN; ADMINISTRATOR AUTHORITY TO SELECT GRANTEES AND DETERMINE AWARDS

(a) Administration of Plan. The Plan shall be administered by the Administrator.

(b) Powers of Administrator. The Administrator shall have the power and authority to grant Awards consistent with the terms of the Plan, including the power and authority:

(i) to select the individuals to whom Awards may from time to time be granted;

(ii) to determine the time or times of grant, and the extent, if any, of Incentive Stock Options, Non-Qualified Stock Options, Stock Appreciation Rights, Restricted Stock Awards, Restricted Stock Units, Unrestricted Stock Awards and Dividend Equivalent Rights, or any combination of the foregoing, granted to any one or more grantees;

(iii) to determine the number of shares of Stock to be covered by any Award;

(iv) to determine and modify from time to time the terms and conditions, including restrictions, not inconsistent with the terms of the Plan, of any Award, which terms and conditions may differ among individual Awards and grantees, and to approve the forms of Award Certificates;

(v) to accelerate at any time the exercisability or vesting of all or any portion of any Award;

(vi) subject to the provisions of Section 5(c), to extend at any time the period in which Stock Options may be exercised;

(i) to cancel any Award provided that a fair compensation is given to the holder whereby the fairness of the compensation shall be determined by the Administrator in its reasonable judgment; and

(vii) at any time to adopt, alter and repeal such rules, guidelines and practices for administration of the Plan and for its own acts and proceedings as it shall deem advisable; to interpret the terms and provisions of the Plan and any Award (including related written instruments); to make all determinations it deems advisable for the administration of the Plan; to decide all disputes arising in connection with the Plan; and to otherwise supervise the administration of the Plan.

All decisions and interpretations of the Administrator shall be binding on all persons, including the Company and Plan grantees.

(c) <u>Delegation of Authority to Grant Awards</u>. Subject to applicable law, the Administrator, in its discretion, may delegate to the Chief Executive Officer of the Company all or part of the Administrator's authority and duties with respect to the granting of Awards to individuals who are (i) not subject to the reporting and other provisions of Section 16 of the US Exchange Act and (ii) not Covered Employees. Any such delegation by the Administrator shall include a limitation as to the amount of Stock underlying Awards that may be granted during the period of the delegation and shall contain guidelines as to the determination of the exercise price and the vesting criteria. The Administrator may revoke or amend the terms of a delegation at any time but such action shall not invalidate any prior actions of the Administrator's delegate or delegates that were consistent with the terms of the Plan.

(d) Award Certificate. Awards under the Plan shall be evidenced by Award Certificates that set forth the terms, conditions and limitations for each Award which may include, without limitation, the term of an Award and the provisions applicable in the event employment or service terminates.

(e) Indemnification. Neither the Board nor the Administrator, nor any member of either or any delegate thereof, shall be liable for any act, omission, interpretation, construction or determination made in good faith in connection with the Plan, and the members of the Board and the Administrator (and any delegate thereof) shall be entitled in all cases to indemnification and reimbursement by the Company in respect of any claim, loss, damage or expense (including, without limitation, reasonable attorneys' fees) arising or resulting therefrom to the fullest extent permitted by law and/or under the Company's articles or bylaws or any directors' and officers' liability insurance coverage which may be in effect from time to time and/or any indemnification agreement between such individual and the Company.

(f) Compliance with Laws or Practices. Notwithstanding any provision of the Plan to the contrary, in order to comply with the laws or practices in countries in which the Company and its Subsidiaries operate or have employees or other individuals eligible for Awards, the Administrator, in its sole discretion, shall have the power and authority to: (i) determine which Subsidiaries shall be covered by the Plan; (ii) determine which individuals are eligible to participate in the Plan; (iii) modify the terms and conditions of any Award granted to individuals; (iv) establish subplans and modify exercise procedures and other terms and procedures, to the extent the Administrator determines such actions to be necessary or advisable (and such subplans and/or modifications shall be attached to this Plan as appendices); provided, however, that no such subplans and/or modifications shall increase the share limitations contained in Section 3(a) hereof; and (v) take any action, before or after an Award is made, that the Administrator determines to be necessary or advisable to obtain approval or comply with any local governmental regulatory exemptions or approvals. Notwithstanding the foregoing, the Administrator may not take any actions hereunder, and no Awards shall be granted, that would violate the Swiss Ordinance against excessive compensation in listed stock corporations (*Verordnung gegen übermässige Vergütungen bei börsenkotierten Aktiengesellschaften*), the US Exchange Act or any other applicable United States securities law, the US Tax Code, or any other applicable United States governing statute or law.

SECTION 3. STOCK ISSUABLE UNDER THE PLAN; MERGERS; SUBSTITUTION

(a) Stock Issuable. The maximum number of shares of Stock reserved and available for issuance under the Plan shall be 4,000,000 shares, plus the number of shares remaining available for issuance under the Company's Amended and Restated 2016 Stock Option and Grant Plan (the "2016 Plan") as of immediately prior to the Effective Date, subject to adjustment as provided in Section 3. For purposes of this limitation, the shares of Stock underlying any Awards under the Plan or any shares of Stock underlying any awards under the Company's 2015 Stock Option and Grant Plan or the 2016 Plan that are forfeited, canceled, held back upon exercise of an Option or settlement of an Award to cover the exercise price or tax withholding, reacquired by the Company prior to vesting, satisfied without the issuance of Stock or otherwise terminated (other than by exercise) shall be added back to the shares of Stock available for issuance under the Plan. In the event the Company repurchases shares of Stock on the open market, such shares shall not be added to the shares of Stock available for issuance under the Plan. Subject to such overall limitations, shares of Stock may be issued up to such maximum number pursuant to any type or types of Award; provided, however, that no more than 16,005,365 shares of the Stock may be issued in the form of Incentive Stock Options. The shares available for issuance under the Plan may be authorized but unissued shares of Stock or shares of Stock reacquired by the Company.

(b) Reserved.

(c) Compliance with Swiss Law. Any grant to a Covered Employee must be within the limits approved by the Shareholders' Meeting and thus be in compliance with the Swiss Ordinance against excessive compensation in listed stock corporations (*Verordnung gegen übermässige Vergütungen bei börsenkotierten Aktiengesellschaften*).

(d) Changes in Stock. Subject to Section 3(e) hereof, if, as a result of any reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split or other similar change in the Company's capital stock, the outstanding shares of Stock are increased or decreased or are exchanged for a different number or kind of shares or other securities of the Company, or additional shares or new or different shares or other securities of the Company or other non-cash assets are distributed with respect to such shares of Stock or other securities, or, if, as a result of any merger or consolidation, sale of all or substantially all of the assets of the Company, the outstanding shares of Stock are converted into or exchanged for securities of the Company or any successor entity (or a parent or subsidiary thereof), the Administrator shall make an appropriate or proportionate adjustment in (i) the maximum number of shares reserved for issuance under the Plan, including the maximum number of shares that may be issued in the form of Incentive Stock Options, (ii) the number and kind of shares or other securities subject to any then outstanding Awards under the Plan, (iii) the repurchase price, if any, per share subject to each outstanding Restricted Stock Award, and (iv) the exercise price for each share subject to any then outstanding Stock Options and Stock Appreciation Rights under the Plan, without changing the aggregate exercise price (i.e., the exercise price multiplied by the number of Stock Options and Stock Appreciation Rights) as to which such Stock Options and Stock Appreciation Rights remain exercisable. The Administrator shall also make equitable or proportionate adjustments in the number of shares subject to outstanding Awards and the exercise price and the terms of outstanding Awards to take into consideration cash dividends paid other than in the ordinary course or any other extraordinary corporate event. The adjustment by the Administrator shall be final, binding and conclusive. No fractional shares of Stock shall be issued under the Plan resulting from any such adjustment, but the Administrator in its discretion may make a cash payment in lieu of fractional shares.

(e) Mergers and Other Transactions. In the case of and subject to the consummation of a Sale Event, the parties thereto may cause the assumption or continuation of Awards theretofore granted by the successor entity, or the substitution of such Awards with new Awards of the successor entity or parent thereof, with appropriate adjustment as to the number and kind of shares and, if appropriate, the per share exercise prices, as such parties shall agree. To the extent the parties to such Sale Event do not provide for the assumption, continuation or substitution of Awards, upon the effective time of the Sale Event, the Plan and all outstanding Awards granted hereunder shall terminate. In such case, except as may be otherwise provided in the relevant Award Certificate, all Options and Stock Appreciation Rights that are not exercisable immediately prior to the effective time of the Sale Event shall become fully exercisable as of the effective time of the Sale Event, all other Awards with time-based vesting, conditions or restrictions shall become fully vested and nonforfeitable as of the effective time of the Sale Event, and all Awards with conditions and restrictions relating to the attainment of performance goals may become vested and nonforfeitable in connection with a Sale Event in the Administrator's discretion or to the extent specified in the relevant Award Certificate. In the event of such termination, (i) the Company shall have the option (in its sole discretion) to make or provide for a payment, in cash or in kind, to the grantees holding Options and Stock Appreciation Rights, in exchange for the cancellation thereof, in an amount equal to the difference between (A) the Sale Price multiplied by the number of shares of Stock subject to outstanding Options and Stock Appreciation Rights (to the extent then exercisable at prices not in excess of the Sale Price) and (B) the aggregate exercise price of all such outstanding Options and Stock Appreciation Rights; or (ii) each grantee shall be permitted, within a specified period of time prior to the consummation of the Sale Event as determined by the Administrator, to exercise all outstanding Options and Stock Appreciation Rights (to the extent then exercisable) held by such grantee. The Company shall also have the option (in its sole discretion) to make or provide for a payment, in cash or in kind, to the grantees holding other Awards in an amount equal to the Sale Price multiplied by the number of vested shares of Stock under such Awards.

SECTION 4. ELIGIBILITY

Grantees under the Plan will be such full or part-time officers and other employees, Non-Employee Directors and Consultants of the Company and its Subsidiaries as are selected from time to time by the Administrator in its sole discretion.

SECTION 5. STOCK OPTIONS

(a) Award of Stock Options. The Administrator may grant Stock Options under the Plan. Any Stock Option granted under the Plan shall be in such form as the Administrator may from time to time approve.

Stock Options granted under the Plan may be either Incentive Stock Options or Non-Qualified Stock Options. Incentive Stock Options may be granted only to employees of the Company or any Subsidiary that is a "subsidiary corporation" within the meaning of Section 424(f) of the US Tax Code. To the extent that any Option does not qualify as an Incentive Stock Option, it shall be deemed a Non-Qualified Stock Option.

Stock Options granted pursuant to this Section 5 shall be subject to the following terms and conditions and shall contain such additional terms and conditions, not inconsistent with the terms of the Plan, as the Administrator shall deem desirable. If the Administrator so determines, Stock Options may be granted in lieu of cash compensation at the optionee's election, subject to such terms and conditions as the Administrator may establish.

(b) Exercise Price. The exercise price per share for the Stock covered by a Stock Option granted pursuant to this Section 5 shall be determined by the Administrator at the time of grant but shall not be less than 100 percent of the Fair Market Value on the date of grant. In the case of an Incentive Stock Option that is granted to a Ten Percent Owner, the option price of such Incentive Stock Option shall be not less than 110 percent of the Fair Market Value on the grant date.

(c) Option Term. The term of each Stock Option shall be fixed by the Administrator, but no Stock Option shall be exercisable more than ten years after the date the Stock Option is granted. In the case of an Incentive Stock Option that is granted to a Ten Percent Owner, the term of such Stock Option shall be no more than five years from the date of grant.

(d) Exercisability; Rights of a Stockholder. Stock Options shall become exercisable at such time or times, whether or not in installments, as shall be determined by the Administrator at or after the grant date. The Administrator may at any time accelerate the exercisability of all or any portion of any Stock Option. An optionee shall have the rights of a stockholder only as to shares acquired upon the exercise of a Stock Option and not as to unexercised Stock Options.

(e) Method of Exercise. Stock Options may be exercised in whole or in part, by giving written or electronic notice of exercise to the Company, specifying the number of shares to be purchased. Payment of the purchase price may be made by one or more of the following methods except to the extent otherwise provided in the Option Award Certificate:

(i) In cash, by certified or bank check or other instrument acceptable to the Administrator;

(ii) Through the delivery (or attestation to the ownership following such procedures as the Company may prescribe) of shares of Stock that are not then subject to restrictions under any Company plan. Such surrendered shares shall be valued at Fair Market Value on the exercise date;

(iii) By the optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company for the purchase price; provided that in the event the optionee chooses to pay the purchase price as so provided, the optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Company shall prescribe as a condition of such payment procedure; or

(iv) With respect to Stock Options that are not Incentive Stock Options, by a "net exercise" arrangement pursuant to which the Company will reduce the number of shares of Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price.

Payment instruments will be received subject to collection. The transfer to the optionee in the share register or the register in book entry form of uncertified securities (*Wertrechte*) of the Company or of the transfer agent of the shares of Stock to be purchased pursuant to the exercise of a Stock Option will be contingent upon receipt from the optionee (or a purchaser acting in his stead in accordance with the provisions of the Stock Option) by the Company of the full purchase price for such shares and the fulfillment of any other requirements contained in the Option Award Certificate or applicable provisions of laws (including the satisfaction of any withholding taxes that the Company is obligated to withhold with respect to the optionee). In the event an optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the optionee upon the exercise of the Stock Option shall be net of the number of attested shares. In the event that the Company establishes, for itself or using the services of a third party, an automated system for the exercise of Stock Options, such as a system using an internet website or interactive voice response, then the paperless exercise of Stock Options may be permitted through the use of such an automated system.

(f) Annual Limit on Incentive Stock Options. To the extent required for "incentive stock option" treatment under Section 422 of the US Tax Code, the aggregate Fair Market Value (determined as of the time of grant) of the shares of Stock with respect to which Incentive Stock Options granted under this Plan and any other plan of the Company or its parent and subsidiary corporations become exercisable for the first time by an optionee during any calendar year shall not exceed $100,000. To the extent that any Stock Option exceeds this limit, it shall constitute a Non-Qualified Stock Option.

SECTION 6. STOCK APPRECIATION RIGHTS

(a) Award of Stock Appreciation Rights. The Administrator may grant Stock Appreciation Rights under the Plan. A Stock Appreciation Right is an Award entitling the recipient to receive shares of Stock (or cash, to the extent explicitly provided for in the applicable Award Certificate) having a value equal to the excess of the Fair Market Value of a share of Stock on the date of exercise over the exercise price of the Stock Appreciation Right multiplied by the number of shares of Stock with respect to which the Stock Appreciation Right shall have been exercised.

(b) Exercise Price of Stock Appreciation Rights. The exercise price of a Stock Appreciation Right shall not be less than 100 percent of the Fair Market Value of the Stock on the date of grant.

(c) Grant and Exercise of Stock Appreciation Rights. Stock Appreciation Rights may be granted by the Administrator independently of any Stock Option granted pursuant to Section 5 of the Plan.

(d) Terms and Conditions of Stock Appreciation Rights. Stock Appreciation Rights shall be subject to such terms and conditions as shall be determined on the date of grant by the Administrator. The term of a Stock Appreciation Right may not exceed ten years. The terms and conditions of each such Award shall be determined by the Administrator, and such terms and conditions may differ among individual Awards and grantees.

SECTION 7. RESTRICTED STOCK AWARDS

(a) Nature of Restricted Stock Awards. The Administrator may grant Restricted Stock Awards under the Plan. A Restricted Stock Award is any Award of Restricted Shares subject to such restrictions and conditions as the Administrator may determine at the time of grant. Conditions may be based on continuing employment (or other service relationship) and/or achievement of pre-established performance goals and objectives.

(b) Rights as a Stockholder. Upon the grant of the Restricted Stock Award and payment of any applicable purchase price, a grantee shall have the rights of a stockholder with respect to the voting of the Restricted Shares and receipt of dividends; provided that if the lapse of restrictions with respect to the Restricted Stock Award is tied to the attainment of performance goals, any dividends paid by the Company during the performance period shall accrue and shall not be paid to the grantee until and to the extent the performance goals are met with respect to the Restricted Stock Award. Unless the Administrator shall otherwise determine, (i) uncertificated Restricted Shares shall be accompanied by a notation in the share register or the register in book entry form of uncertified securities (*Wertrechte*) or the transfer agent to the effect that they are subject to forfeiture until such Restricted Shares are vested as provided in Section 7(d) below, and (ii) certificated Restricted Shares shall remain in the possession of the Company until such Restricted Shares are vested as provided in Section 7(d) below, and the grantee shall be required, as a condition of the grant, to deliver to the Company such instruments of transfer as the Administrator may prescribe.

(c) Restrictions. Restricted Shares may not be sold, assigned, transferred, pledged or otherwise encumbered or disposed of except as specifically provided herein or in the Restricted Stock Award Certificate. Except as may otherwise be provided by the Administrator either in the Award Certificate or, subject to Section 15 below, in writing after the Award is issued, if a grantee's employment (or other service relationship) with the Company and its Subsidiaries terminates for any reason, any Restricted Shares that have not vested at the time of termination shall automatically and without any requirement of notice to such grantee from or other action by or on behalf of, the Company be deemed to have been reacquired by the Company at its original purchase price (if any) from such grantee or such grantee's legal representative simultaneously with such termination of employment (or other service relationship), and thereafter shall cease to represent any ownership of the Company by the grantee or rights of the grantee as a stockholder. Following such deemed reacquisition of Restricted Shares that are represented by physical certificates, a grantee shall surrender such certificates to the Company upon request without consideration.

(d) Vesting of Restricted Shares. The Administrator at the time of grant shall specify the date or dates and/or the attainment of pre-established performance goals, objectives and other conditions on which the non-transferability of the Restricted Shares and the Company's right of repurchase or forfeiture shall lapse. Subsequent to such date or dates and/or the attainment of such pre-established performance goals, objectives and other conditions, the shares on which all restrictions have lapsed shall no longer be Restricted Shares and shall be deemed "vested."

SECTION 8. RESTRICTED STOCK UNITS

(a) Nature of Restricted Stock Units. The Administrator may grant Restricted Stock Units under the Plan. A Restricted Stock Unit is an Award of stock units that may be settled in shares of Stock (or cash, to the extent explicitly provided for in the applicable Award Certificate) upon the satisfaction of such restrictions and conditions at the time of grant. Conditions may be based on continuing employment (or other service relationship) and/or achievement of pre-established performance goals and objectives. The terms and conditions of each such Award shall be determined by the Administrator, and such terms and conditions may differ among individual Awards and grantees. Except in the case of Restricted Stock Units with a deferred settlement date that complies with Section 409A, at the end of the vesting period, the Restricted Stock Units, to the extent vested, shall be settled in the form of shares of Stock. Restricted Stock Units with deferred settlement dates are subject to Section 409A and shall contain such additional terms and conditions as the Administrator shall determine in its sole discretion in order to comply with the requirements of Section 409A.

(b) Election to Receive Restricted Stock Units in Lieu of Compensation. The Administrator may, in its sole discretion, permit a grantee to elect to receive a portion of future cash compensation otherwise due to such grantee in the form of an award of Restricted Stock Units. Any such election shall be made in writing and shall be delivered to the Company no later than the date specified by the Administrator and in accordance with Section 409A and such other rules and procedures established by the Administrator. Any such future cash compensation that the grantee elects to defer shall be converted to a fixed number of Restricted Stock Units based on the Fair Market Value of Stock on the date the compensation would otherwise have been paid to the grantee if such payment had not been deferred as provided herein. The Administrator shall have the sole right to determine whether and under what circumstances to permit such elections and to impose such limitations and other terms and conditions thereon as the Administrator deems appropriate. Any Restricted Stock Units that are elected to be received in lieu of cash compensation shall be fully vested, unless otherwise provided in the Award Certificate.

(c) Rights as a Stockholder. A grantee shall have the rights as a stockholder only as to shares of Stock acquired by the grantee upon settlement of Restricted Stock Units; provided, however, that the grantee may be credited with Dividend Equivalent Rights with respect to the stock units underlying his Restricted Stock Units, subject to the provisions of Section 10 and such terms and conditions as the Administrator may determine.

(d) Termination. Except as may otherwise be provided by the Administrator either in the Award Certificate or, subject to Section 15 below, in writing after the Award is issued, a grantee's right in all Restricted Stock Units that have not vested shall automatically terminate upon the grantee's termination of employment (or cessation of service relationship) with the Company and its Subsidiaries for any reason.

SECTION 9. UNRESTRICTED STOCK AWARDS

Grant or Sale of Unrestricted Stock. The Administrator may grant (or sell at par value or such higher purchase price determined by the Administrator) an Unrestricted Stock Award under the Plan. An Unrestricted Stock Award is an Award pursuant to which the grantee may receive shares of Stock free of any restrictions under the Plan. Unrestricted Stock Awards may be granted in respect of past services or other valid consideration, or in lieu of cash compensation due to such grantee.

SECTION 10. DIVIDEND EQUIVALENT RIGHTS

(a) Dividend Equivalent Rights. The Administrator may grant Dividend Equivalent Rights under the Plan. A Dividend Equivalent Right is an Award entitling the grantee to receive credits based on cash dividends that would have been paid on the shares of Stock specified in the Dividend Equivalent Right (or other Award to which it relates) if such shares had been issued to the grantee. A Dividend Equivalent Right may be granted hereunder to any grantee as a component of an award of Restricted Stock Units or as a freestanding award. The terms and conditions of Dividend Equivalent Rights shall be specified in the Award Certificate. Dividend equivalents credited to the holder of a Dividend Equivalent Right may be paid currently or may be deemed to be reinvested in additional shares of Stock, which may thereafter accrue additional equivalents. Any such reinvestment shall be at Fair Market Value on the date of reinvestment or such other price as may then apply under a dividend reinvestment plan sponsored by the Company, if any. Dividend Equivalent Rights may be settled in cash or shares of Stock or a combination thereof, in a single installment or installments. A Dividend Equivalent Right granted as a component of an Award of Restricted Stock Units shall provide that such Dividend Equivalent Right shall be settled only upon settlement or payment of, or lapse of restrictions on, such other Award, and that such Dividend Equivalent Right shall expire or be forfeited or annulled under the same conditions as such other Award.

(b) Termination. Except as may otherwise be provided by the Administrator either in the Award Certificate or, subject to Section 15 below, in writing after the Award is issued, a grantee's rights in all Dividend Equivalent Rights shall automatically terminate upon the grantee's termination of employment (or cessation of service relationship) with the Company and its Subsidiaries for any reason.

SECTION 11. TRANSFERABILITY OF AWARDS

(a) Transferability. Except as provided in Section 11(b) below, during a grantee's lifetime, his or her Awards shall be exercisable only by the grantee, or by the grantee's legal representative or guardian in the event of the grantee's incapacity. No Awards shall be sold, assigned, transferred or otherwise encumbered or disposed of by a grantee other than by will or by the laws of descent and distribution or pursuant to a domestic relations order. No Awards shall be subject, in whole or in part, to attachment, execution, or levy of any kind, and any purported transfer in violation hereof shall be null and void.

(b) Administrator Action. Notwithstanding Section 11(a), the Administrator, in its discretion, may provide either in the Award Certificate regarding a given Award or by subsequent written approval that the grantee (who is an employee or director) may transfer his or her Non-Qualified Stock Options to his or her immediate family members, to trusts for the benefit of such family members, or to partnerships in which such family members are the only partners, provided that the transferee agrees in writing with the Company to be bound by all of the terms and conditions of this Plan and the applicable Award. In no event may an Award be transferred by a grantee for value.

(c) Family Member. For purposes of Section 11(b), "family member" shall mean a grantee's child, stepchild, grandchild, parent, stepparent, grandparent, spouse, former spouse, sibling, niece, nephew, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including adoptive relationships, any person sharing the grantee's household (other than a tenant of the grantee), a trust in which these persons (or the grantee) have more than 50 percent of the beneficial interest, a foundation in which these persons (or the grantee) control the management of assets, and any other entity in which these persons (or the grantee) own more than 50 percent of the voting interests.

(d) Designation of Beneficiary. To the extent permitted by the Company, each grantee to whom an Award has been made under the Plan may designate a beneficiary or beneficiaries to exercise any Award or receive any payment under any Award payable on or after the grantee's death. Any such designation shall be on a form provided for that purpose by the Administrator and shall not be effective until received by the Administrator. If no beneficiary has been designated by a deceased grantee, or if the designated beneficiaries have predeceased the grantee, the beneficiary shall be the grantee's estate.

SECTION 12. TAX AND SOCIAL SECURITY WITHHOLDING

(a) Payment by Grantee. Each grantee shall, no later than the date as of which the value of an Award or of any Stock or other amounts received thereunder first becomes includable in the gross income of the grantee for income tax and, if applicable, social security purposes, pay to the Company, or make arrangements satisfactory to the Administrator regarding payment of, any Federal, state, or local taxes of any kind required by law to be withheld by the Company with respect to such income. The Company and its Subsidiaries shall, to the extent permitted by law, have the right to deduct any such taxes from any payment of any kind otherwise due to the grantee. The Company's obligation to deliver evidence of book entry (or stock certificates) to any grantee is subject to and conditioned on tax withholding obligations being satisfied by the grantee.

(b) Payment in Stock. Subject to approval by the Administrator, a grantee may elect to have the Company's required tax and, if applicable, social security withholding obligation satisfied, in whole or in part, by authorizing the Company to withhold from shares of Stock to be issued pursuant to any Award a number of shares with an aggregate Fair Market Value (as of the date the withholding is effected) that would satisfy the withholding amount due; provided, however, that the amount withheld does not exceed the maximum statutory tax rate or such lesser amount as is necessary to avoid adverse accounting treatment. The Administrator may also require Awards to be subject to mandatory share withholding up to the required withholding amount. For purposes of share withholding, the Fair Market Value of withheld shares shall be determined in the same manner as the value of Stock includible in income of the Participants.

SECTION 13. SECTION 409A AWARDS

To the extent that any Award is determined to constitute "nonqualified deferred compensation" within the meaning of Section 409A (a "409A Award"), the Award shall be subject to such additional rules and requirements as specified by the Administrator from time to time in order to comply with Section 409A. In this regard, if any amount under a 409A Award is payable upon a "separation from service" (within the meaning of Section 409A) to a grantee who is then considered a "specified employee" (within the meaning of Section 409A), then no such payment shall be made prior to the date that is the earlier of (i) six months and one day after the grantee's separation from service, or (ii) the grantee's death, but only to the extent such delay is necessary to prevent such payment from being subject to interest, penalties and/or additional tax imposed pursuant to Section 409A. Further, the settlement of any such Award may not be accelerated except to the extent permitted by Section 409A.

SECTION 14. TERMINATION OF EMPLOYMENT, TRANSFER, LEAVE OF ABSENCE, ETC.

(a) Termination of Employment. If the grantee's employer ceases to be a Subsidiary, the grantee shall be deemed to have terminated employment for purposes of the Plan.

(b) For purposes of the Plan, the following events shall not be deemed a termination of employment:

(i) a transfer to the employment of the Company from a Subsidiary or from the Company to a Subsidiary, or from one Subsidiary to another; or

(ii) an approved leave of absence for military service or sickness, or for any other purpose approved by the Company, if the employee's right to re-employment is guaranteed either by a statute or by contract or under the policy pursuant to which the leave of absence was granted or if the Administrator otherwise so provides in writing.

SECTION 15. AMENDMENTS AND TERMINATION

The Board may, at any time, amend or discontinue the Plan and the Administrator may, at any time, amend or cancel any outstanding Award for the purpose of satisfying changes in law or for any other lawful purpose, but no such action shall adversely affect rights under any outstanding Award without the holder's consent. Except as provided in Section 3(d) or 3(e), without prior stockholder approval, in no event may the Administrator exercise its discretion to reduce the exercise price of outstanding Stock Options or Stock Appreciation Rights or effect repricing through cancellation and re-grants or cancellation of Stock Options or Stock Appreciation Rights in exchange for cash or other Awards. To the extent required under the rules of any securities exchange or market system on which the Stock is listed, or to the extent determined by the Administrator to be required by the US Tax Code to ensure that Incentive Stock Options granted under the Plan are qualified under Section 422 of the US Tax Code, Plan amendments shall be subject to approval by the Company stockholders entitled to vote at a meeting of stockholders. Nothing in this Section 15 shall limit the Administrator's authority to take any action permitted pursuant to Section 3(d) or 3(e).

SECTION 16. STATUS OF PLAN

With respect to the portion of any Award that has not been exercised and any payments in cash, Stock or other consideration not received by a grantee, a grantee shall have no rights greater than those of a general creditor of the Company unless the Administrator shall otherwise expressly determine in connection with any Award or Awards. In its sole discretion, the Administrator may authorize the creation of trusts or other arrangements to meet the Company's obligations to deliver Stock or make payments with respect to Awards hereunder, provided that the existence of such trusts or other arrangements is consistent with the foregoing sentence.

SECTION 17. GENERAL PROVISIONS

(a) No Distribution. The Administrator may require each person acquiring Stock pursuant to an Award to represent to and agree with the Company in writing that such person is acquiring the shares without a view to distribution thereof.

(b) No Delivery of Stock Certificates. No Stock certificates to grantees under the Plan shall be delivered, as all shares are recorded in the Company's share register or in book entry form as uncertified securities (*Wertrechte*).

(c) Stockholder Rights. Until a grantee has been recorded in the Company's share register, no right to vote or receive dividends or any other rights of a stockholder will exist with respect to shares of Stock to be issued in connection with an Award, notwithstanding the exercise of a Stock Option or any other action by the grantee with respect to an Award.

(d) Other Compensation Arrangements; No Employment Rights. Nothing contained in this Plan shall prevent the Board from adopting other or additional compensation arrangements, including trusts, and such arrangements may be either generally applicable or applicable only in specific cases. The adoption of this Plan and the grant of Awards do not confer upon any employee any right to continued employment with the Company or any Subsidiary.

(e) Trading Policy Restrictions. Option exercises and other Awards under the Plan shall be subject to the Company’s insider trading policies and procedures, as in effect from time to time.

(f) Clawback Policy. Awards under the Plan shall be subject to the Company’s clawback policy, as in effect from time to time.

SECTION 18. EFFECTIVE DATE OF PLAN

This Plan shall become effective upon shareholder approval in accordance with applicable law, the Company’s articles of association, and applicable stock exchange rules. No grants of Stock Options and other Awards may be made hereunder after the tenth anniversary of the Effective Date and no grants of Incentive Stock Options may be made hereunder after the tenth anniversary of the date the Plan is approved by the Board.

SECTION 19. GOVERNING LAW AND JURISDICTION

This Plan and all Awards and actions taken thereunder shall be governed by, and construed in accordance with, the internal laws of Switzerland, and exclusive place of jurisdiction shall be Basel, Switzerland.

DATE APPROVED BY BOARD OF DIRECTORS:

DATE APPROVED BY STOCKHOLDERS:

INCENTIVE STOCK OPTION AGREEMENT UNDER THE CRISPR THERAPEUTICS AG 2018 STOCK OPTION AND INCENTIVE PLAN

Name of Optionee:	______________________________
No. of Option Shares:	______________________________
Option Exercise Price per Share:	$_____________________________
Grant Date:	______________________________
Expiration Date:	______________________________

Pursuant to the CRISPR Therapeutics AG 2018 Stock Option and Incentive Plan as amended through the date hereof (the "Plan"), CRISPR Therapeutics AG (the "Company") hereby grants to the Optionee named above an option (the "Stock Option") to purchase on or prior to the Expiration Date specified above all or part of the number of shares of Common Stock, par value CHF 0.03 per share (the "Stock"), of the Company specified above at the Option Exercise Price per Share specified above subject to the terms and conditions set forth herein and in the Plan.

1. Exercisability Schedule. No portion of this Stock Option may be exercised until such portion shall have become exercisable. Except as set forth below, and subject to the discretion of the Administrator (as defined in Section 2 of the Plan) to accelerate the exercisability schedule hereunder, this Stock Option shall be exercisable with respect to the following number of Option Shares on the dates indicated so long as the Optionee remains an employee of the Company or a Subsidiary on such dates:

Incremental Number of Option Shares Exercisable*	Exercisability Date
_____________ (___%)	____________
_____________ (___%)	____________
_____________ (___%)	____________
_____________ (___%)	____________
_____________ (___%)	____________

* Max. of $100,000 per yr.

Once exercisable, this Stock Option shall continue to be exercisable at any time or times prior to the close of business on the Expiration Date, subject to the provisions hereof and of the Plan.

2. Manner of Exercise.

(a) The Optionee may exercise this Stock Option only in the following manner: from time to time on or prior to the Expiration Date of this Stock Option, the Optionee may give written notice to the Administrator of his or her election to purchase some or all of the Option Shares purchasable at the time of such notice. This notice shall specify the number of Option Shares to be purchased.

Payment of the purchase price for the Option Shares may be made by one or more of the following methods: (i) in cash, by certified or bank check or other instrument acceptable to the Administrator; (ii) through the delivery (or attestation to the ownership) of shares of Stock that have been purchased by the Optionee on the open market or that are beneficially owned by the Optionee and are not then subject to any restrictions under any Company plan and that otherwise satisfy any holding periods as may be required by the Administrator; or (iii) by the Optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company to pay the option purchase price, provided that in the event the Optionee chooses to pay the option purchase price as so provided, the Optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Administrator shall prescribe as a condition of such payment procedure; or (iv) a combination of (i), (ii) and (iii) above. Payment instruments will be received subject to collection.

The transfer to the Optionee on the records of the Company or of the transfer agent of the Option Shares will be contingent upon (i) the Company's receipt from the Optionee of the full purchase price for the Option Shares, as set forth above, (ii) the fulfillment of any other requirements contained herein or in the Plan or in any other agreement or provision of laws, and (iii) the receipt by the Company of any agreement, statement or other evidence that the Company may require to satisfy itself that the issuance of Stock to be purchased pursuant to the exercise of Stock Options under the Plan and any subsequent resale of the shares of Stock will be in compliance with applicable laws and regulations. In the event the Optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the Optionee upon the exercise of the Stock Option shall be net of the Shares attested to.

(b) The shares of Stock purchased upon exercise of this Stock Option shall be transferred to the Optionee on the records of the Company or of the transfer agent upon compliance to the satisfaction of the Administrator with all requirements under applicable laws or regulations in connection with such transfer and with the requirements hereof and of the Plan. The determination of the Administrator as to such compliance shall be final and binding on the Optionee. The Optionee shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Stock subject to this Stock Option unless and until this Stock Option shall have been exercised pursuant to the terms hereof, the Company or the transfer agent shall have transferred the shares to the Optionee, and the Optionee's name shall have been entered as the stockholder of record on the books of the Company. Thereupon, the Optionee shall have full voting, dividend and other ownership rights with respect to such shares of Stock.

(c) The minimum number of shares with respect to which this Stock Option may be exercised at any one time shall be 100 shares, unless the number of shares with respect to which this Stock Option is being exercised is the total number of shares subject to exercise under this Stock Option at the time.

(d) Notwithstanding any other provision hereof or of the Plan, no portion of this Stock Option shall be exercisable after the Expiration Date hereof.

3. Termination of Employment. If the Optionee's employment by the Company or a Subsidiary (as defined in the Plan) is terminated, the period within which to exercise the Stock Option may be subject to earlier termination as set forth below.

(a) Termination Due to Death. If the Optionee's employment terminates by reason of the Optionee's death, any portion of this Stock Option outstanding on such date, to the extent exercisable on the date of death, may thereafter be exercised by the Optionee's legal representative or legatee for a period of 12 months from the date of death or until the Expiration Date, if earlier. Any portion of this Stock Option that is not exercisable on the date of death shall terminate immediately and be of no further force or effect.

(b) Termination Due to Disability. If the Optionee's employment terminates by reason of the Optionee's disability (as determined by the Administrator), any portion of this Stock Option outstanding on such date, to the extent exercisable on the date of such termination of employment, may thereafter be exercised by the Optionee for a period of 12 months from the date of disability or until the Expiration Date, if earlier. Any portion of this Stock Option that is not exercisable on the date of disability shall terminate immediately and be of no further force or effect.

(c) Termination for Cause. If the Optionee's employment terminates for Cause, any portion of this Stock Option outstanding on such date shall terminate immediately and be of no further force and effect. For purposes hereof, "Cause" shall mean, unless otherwise provided in an employment agreement between the Company and the Optionee, a determination by the Administrator that the Optionee shall be dismissed as a result of (i) any material breach by the Optionee of any agreement between the Optionee and the Company; (ii) the conviction of, indictment for or plea of nolo contendere by the Optionee to a felony or a crime involving moral turpitude; or (iii) any material misconduct or willful and deliberate non-performance (other than by reason of disability) by the Optionee of the Optionee's duties to the Company.

(d) Other Termination. If the Optionee's employment terminates for any reason other than the Optionee's death, the Optionee's disability, or Cause, and unless otherwise determined by the Administrator, any portion of this Stock Option outstanding on such date may be exercised, to the extent exercisable on the date of termination, for a period of three months from the date of termination or until the Expiration Date, if earlier. Any portion of this Stock Option that is not exercisable on the date of termination shall terminate immediately and be of no further force or effect.

The Administrator's determination of the reason for termination of the Optionee's employment shall be conclusive and binding on the Optionee and his or her representatives or legatees.

4. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Stock Option shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

5. Transferability. This Agreement is personal to the Optionee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution. This Stock Option is exercisable, during the Optionee's lifetime, only by the Optionee, and thereafter, only by the Optionee's legal representative or legatee.

6. Status of the Stock Option. This Stock Option is intended to qualify as an "incentive stock option" under Section 422 of the Internal Revenue Code of 1986, as amended (the "Code"), but the Company does not represent or warrant that this Stock Option qualifies as such. The Optionee should consult with his or her own tax advisors regarding the tax effects of this Stock Option and the requirements necessary to obtain favorable income tax treatment under Section 422 of the Code, including, but not limited to, holding period requirements. To the extent any portion of this Stock Option does not so qualify as an "incentive stock option," such portion shall be deemed to be a non-qualified stock option. If the Optionee intends to dispose or does dispose (whether by sale, gift, transfer or otherwise) of any Option Shares within the one-year period beginning on the date after the transfer of such shares to him or her, or within the two-year period beginning on the day after the grant of this Stock Option, he or she will so notify the Company within 30 days after such disposition.

7. Tax Withholding. The Optionee shall, not later than the date as of which the exercise of this Stock Option becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event. The Company shall have the authority to cause the required tax withholding obligation to be satisfied, in whole or in part, by withholding from shares of Stock to be issued to the Optionee a number of shares of Stock with an aggregate Fair Market Value that would satisfy the withholding amount due.

8. No Obligation to Continue Employment. Neither the Company nor any Subsidiary is obligated by or as a result of the Plan or this Agreement to continue the Optionee in employment and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Subsidiary to terminate the employment of the Optionee at any time.

9. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Stock Option and supersedes all prior agreements and discussions between the parties concerning such subject matter.

10. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the “Relevant Companies”) may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the “Relevant Information”). By entering into this Agreement, the Optionee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Optionee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Optionee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

11. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Optionee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

CRISPR THERAPEUTICS AG

By: ____________________________
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company’s instructions to the Optionee (including through an online acceptance process) is acceptable.

Dated: ________________________ ____________________________
Optionee’s Signature

Optionee’s name and address:
____
____
____

NON-QUALIFIED STOCK OPTION AGREEMENT FOR COMPANY EMPLOYEES UNDER THE CRISPR THERAPEUTICS AG 2018 STOCK OPTION AND INCENTIVE PLAN

Name of Optionee:	______________________________
No. of Option Shares:	________________________
Option Exercise Price per Share:	$_______________________
Grant Date:	________________________
Expiration Date:	________________________

Pursuant to the CRISPR Therapeutics AG 2018 Stock Option and Incentive Plan as amended through the date hereof (the "Plan"), CRISPR Therapeutics AG (the "Company") hereby grants to the Optionee named above an option (the "Stock Option") to purchase on or prior to the Expiration Date specified above all or part of the number of shares of Common Stock, par value CHF 0.03 per share (the "Stock") of the Company specified above at the Option Exercise Price per Share specified above subject to the terms and conditions set forth herein and in the Plan. This Stock Option is not intended to be an "incentive stock option" under Section 422 of the Internal Revenue Code of 1986, as amended.

1. Exercisability Schedule. No portion of this Stock Option may be exercised until such portion shall have become exercisable. Except as set forth below, and subject to the discretion of the Administrator (as defined in Section 2 of the Plan) to accelerate the exercisability schedule hereunder, this Stock Option shall be exercisable with respect to the following number of Option Shares on the dates indicated so long as Optionee remains an employee of the Company or a Subsidiary on such dates:

Incremental Number of Option Shares Exercisable	Exercisability Date
_____________ (___%)	____________
_____________ (___%)	____________
_____________ (___%)	____________
_____________ (___%)	____________
_____________ (___%)	____________

Once exercisable, this Stock Option shall continue to be exercisable at any time or times prior to the close of business on the Expiration Date, subject to the provisions hereof and of the Plan.

2. Manner of Exercise.

(a) The Optionee may exercise this Stock Option only in the following manner: from time to time on or prior to the Expiration Date of this Stock Option, the Optionee may give written notice to the Administrator of his or her election to purchase some or all of the Option Shares purchasable at the time of such notice. This notice shall specify the number of Option Shares to be purchased.

Payment of the purchase price for the Option Shares may be made by one or more of the following methods: (i) in cash, by certified or bank check or other instrument acceptable to the Administrator; (ii) through the delivery (or attestation to the ownership) of shares of Stock that have been purchased by the Optionee on the open market or that are beneficially owned by the Optionee and are not then subject to any restrictions under any Company plan and that otherwise satisfy any holding periods as may be required by the Administrator; (iii) by the Optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company to pay the option purchase price, provided that in the event the Optionee chooses to pay the option purchase price as so provided, the Optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Administrator shall prescribe as a condition of such payment procedure; (iv) by a “net exercise” arrangement pursuant to which the Company will reduce the number of shares of Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price; or (v) a combination of (i), (ii), (iii) and (iv) above. Payment instruments will be received subject to collection.

The transfer to the Optionee on the records of the Company or of the transfer agent of the Option Shares will be contingent upon (i) the Company’s receipt from the Optionee of the full purchase price for the Option Shares, as set forth above, (ii) the fulfillment of any other requirements contained herein or in the Plan or in any other agreement or provision of laws, and (iii) the receipt by the Company of any agreement, statement or other evidence that the Company may require to satisfy itself that the issuance of Stock to be purchased pursuant to the exercise of Stock Options under the Plan and any subsequent resale of the shares of Stock will be in compliance with applicable laws and regulations. In the event the Optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the Optionee upon the exercise of the Stock Option shall be net of the Shares attested to.

(b) The shares of Stock purchased upon exercise of this Stock Option shall be transferred to the Optionee on the records of the Company or of the transfer agent upon compliance to the satisfaction of the Administrator with all requirements under applicable laws or regulations in connection with such transfer and with the requirements hereof and of the Plan. The determination of the Administrator as to such compliance shall be final and binding on the Optionee. The Optionee shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Stock subject to this Stock Option unless and until this Stock Option shall have been exercised pursuant to the terms hereof, the Company or the transfer agent shall have transferred the shares to the Optionee, and the Optionee’s name shall have been entered as the stockholder of record on the books of the Company. Thereupon, the Optionee shall have full voting, dividend and other ownership rights with respect to such shares of Stock.

(c) The minimum number of shares with respect to which this Stock Option may be exercised at any one time shall be 100 shares, unless the number of shares with respect to which this Stock Option is being exercised is the total number of shares subject to exercise under this Stock Option at the time.

(d) Notwithstanding any other provision hereof or of the Plan, no portion of this Stock Option shall be exercisable after the Expiration Date hereof.

3. Termination of Employment. If the Optionee's employment by the Company or a Subsidiary (as defined in the Plan) is terminated, the period within which to exercise the Stock Option may be subject to earlier termination as set forth below.

(a) Termination Due to Death. If the Optionee's employment terminates by reason of the Optionee's death, any portion of this Stock Option outstanding on such date, to the extent exercisable on the date of death, may thereafter be exercised by the Optionee's legal representative or legatee for a period of 12 months from the date of death or until the Expiration Date, if earlier. Any portion of this Stock Option that is not exercisable on the date of death shall terminate immediately and be of no further force or effect.

(b) Termination Due to Disability. If the Optionee's employment terminates by reason of the Optionee's disability (as determined by the Administrator), any portion of this Stock Option outstanding on such date, to the extent exercisable on the date of such termination of employment, may thereafter be exercised by the Optionee for a period of 12 months from the date of disability or until the Expiration Date, if earlier. Any portion of this Stock Option that is not exercisable on the date of disability shall terminate immediately and be of no further force or effect.

(c) Termination for Cause. If the Optionee's employment terminates for Cause, any portion of this Stock Option outstanding on such date shall terminate immediately and be of no further force and effect. For purposes hereof, "Cause" shall mean, unless otherwise provided in an employment agreement between the Company and the Optionee, a determination by the Administrator that the Optionee shall be dismissed as a result of (i) any material breach by the Optionee of any agreement between the Optionee and the Company; (ii) the conviction of, indictment for or plea of nolo contendere by the Optionee to a felony or a crime involving moral turpitude; or (iii) any material misconduct or willful and deliberate non-performance (other than by reason of disability) by the Optionee of the Optionee's duties to the Company.

(d) Other Termination. If the Optionee's employment terminates for any reason other than the Optionee's death, the Optionee's disability or Cause, and unless otherwise determined by the Administrator, any portion of this Stock Option outstanding on such date may be exercised, to the extent exercisable on the date of termination, for a period of three months from the date of termination or until the Expiration Date, if earlier. Any portion of this Stock Option that is not exercisable on the date of termination shall terminate immediately and be of no further force or effect.

The Administrator's determination of the reason for termination of the Optionee's employment shall be conclusive and binding on the Optionee and his or her representatives or legatees.

4. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Stock Option shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

5. Transferability. This Agreement is personal to the Optionee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution. This Stock Option is exercisable, during the Optionee's lifetime, only by the Optionee, and thereafter, only by the Optionee's legal representative or legatee.

6. Tax Withholding. The Optionee shall, not later than the date as of which the exercise of this Stock Option becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event. The Company shall have the authority to cause the required tax withholding obligation to be satisfied, in whole or in part, by withholding from shares of Stock to be issued to the Optionee a number of shares of Stock with an aggregate Fair Market Value that would satisfy the withholding amount due.

7. No Obligation to Continue Employment. Neither the Company nor any Subsidiary is obligated by or as a result of the Plan or this Agreement to continue the Optionee in employment and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Subsidiary to terminate the employment of the Optionee at any time.

8. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Stock Option and supersedes all prior agreements and discussions between the parties concerning such subject matter.

9. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the "Relevant Companies") may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the "Relevant Information"). By entering into this Agreement, the Optionee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Optionee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Optionee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

10. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Optionee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

CRISPR THERAPEUTICS AG

By: ______________________________
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Optionee (including through an online acceptance process) is acceptable.

Dated: ______________________________ ______________________________
Optionee's Signature

Optionee's name and address:
____
____
____

Exhibit 10.20.3

NON-QUALIFIED STOCK OPTION AGREEMENT
FOR NON-EMPLOYEE DIRECTORS
UNDER THE CRISPR THERAPEUTICS AG
2018 STOCK OPTION AND INCENTIVE PLAN

Name of Optionee:	______________________________
No. of Option Shares:	__________________
Option Exercise Price per Share:	$__________________
Grant Date:	__________________
Expiration Date:	__________________

Pursuant to the CRISPR Therapeutics AG 2018 Stock Option and Incentive Plan as amended through the date hereof (the "Plan"), CRISPR Therapeutics AG (the "Company") hereby grants to the Optionee named above, who is a Director of the Company but is not an employee of the Company, an option (the "Stock Option") to purchase on or prior to the Expiration Date specified above all or part of the number of shares of Common Stock, par value CHF 0.03 per share (the "Stock"), of the Company specified above at the Option Exercise Price per Share specified above subject to the terms and conditions set forth herein and in the Plan. This Stock Option is not intended to be an "incentive stock option" under Section 422 of the Internal Revenue Code of 1986, as amended.

1. Exercisability Schedule. No portion of this Stock Option may be exercised until such portion shall have become exercisable. Except as set forth below, and subject to the discretion of the Administrator (as defined in Section 2 of the Plan) to accelerate the exercisability schedule hereunder, this Stock Option shall be exercisable with respect to the following number of Option Shares on the dates indicated so long as the Optionee remains in service as a member of the Board on such dates:

Incremental Number of Option Shares Exercisable	Exercisability Date
______________ (___%)	_____________
______________ (___%)	_____________
______________ (___%)	_____________
______________ (___%)	_____________
______________ (___%)	_____________

Once exercisable, this Stock Option shall continue to be exercisable at any time or times prior to the close of business on the Expiration Date, subject to the provisions hereof and of the Plan.

2. Manner of Exercise.

(a) The Optionee may exercise this Stock Option only in the following manner: from time to time on or prior to the Expiration Date of this Stock Option, the Optionee may give written notice to the Administrator of his or her election to purchase some or all of the Option Shares purchasable at the time of such notice. This notice shall specify the number of Option Shares to be purchased.

Payment of the purchase price for the Option Shares may be made by one or more of the following methods: (i) in cash, by certified or bank check or other instrument acceptable to the Administrator; (ii) through the delivery (or attestation to the ownership) of shares of Stock that have been purchased by the Optionee on the open market or that are beneficially owned by the Optionee and are not then subject to any restrictions under any Company plan and that otherwise satisfy any holding periods as may be required by the Administrator; (iii) by the Optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company to pay the option purchase price, provided that in the event the Optionee chooses to pay the option purchase price as so provided, the Optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Administrator shall prescribe as a condition of such payment procedure; (iv) by a “net exercise” arrangement pursuant to which the Company will reduce the number of shares of Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price; or (v) a combination of (i), (ii), (iii) and (iv) above. Payment instruments will be received subject to collection.

The transfer to the Optionee on the records of the Company or of the transfer agent of the Option Shares will be contingent upon (i) the Company’s receipt from the Optionee of the full purchase price for the Option Shares, as set forth above, (ii) the fulfillment of any other requirements contained herein or in the Plan or in any other agreement or provision of laws, and (iii) the receipt by the Company of any agreement, statement or other evidence that the Company may require to satisfy itself that the issuance of Stock to be purchased pursuant to the exercise of Stock Options under the Plan and any subsequent resale of the shares of Stock will be in compliance with applicable laws and regulations. In the event the Optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the Optionee upon the exercise of the Stock Option shall be net of the Shares attested to.

(b) The shares of Stock purchased upon exercise of this Stock Option shall be transferred to the Optionee on the records of the Company or of the transfer agent upon compliance to the satisfaction of the Administrator with all requirements under applicable laws or regulations in connection with such transfer and with the requirements hereof and of the Plan. The determination of the Administrator as to such compliance shall be final and binding on the Optionee. The Optionee shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Stock subject to this Stock Option unless and until this

Stock Option shall have been exercised pursuant to the terms hereof, the Company or the transfer agent shall have transferred the shares to the Optionee, and the Optionee's name shall have been entered as the stockholder of record on the books of the Company. Thereupon, the Optionee shall have full voting, dividend and other ownership rights with respect to such shares of Stock.

(c) The minimum number of shares with respect to which this Stock Option may be exercised at any one time shall be 100 shares, unless the number of shares with respect to which this Stock Option is being exercised is the total number of shares subject to exercise under this Stock Option at the time.

(d) Notwithstanding any other provision hereof or of the Plan, no portion of this Stock Option shall be exercisable after the Expiration Date hereof.

3. Termination as Director. If the Optionee ceases to be a Director of the Company, the period within which to exercise the Stock Option may be subject to earlier termination as set forth below.

(a) Termination Due to Death. If the Optionee's service as a Director terminates by reason of the Optionee's death, any portion of this Stock Option outstanding on such date, to the extent exercisable on the date of death, may thereafter be exercised by the Optionee's legal representative or legatee for a period of 12 months from the date of death or until the Expiration Date, if earlier. Any portion of this Stock Option that is not exercisable on the date of death shall terminate immediately and be of no further force or effect.

(b) Other Termination. If the Optionee ceases to be a Director for any reason other than the Optionee's death, any portion of this Stock Option outstanding on such date may be exercised, to the extent exercisable on the date the Optionee ceased to be a Director, for a period of six months from the date the Optionee ceased to be a Director or until the Expiration Date, if earlier. Any portion of this Stock Option that is not exercisable on the date the Optionee ceases to be a Director shall terminate immediately and be of no further force or effect.

4. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Stock Option shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

5. Transferability. This Agreement is personal to the Optionee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution. This Stock Option is exercisable, during the Optionee's lifetime, only by the Optionee, and thereafter, only by the Optionee's legal representative or legatee.

6. No Obligation to Continue as a Director. Neither the Plan nor this Stock Option confers upon the Optionee any rights with respect to continuance as a Director.

7. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Stock Option and supersedes all prior agreements and discussions between the parties concerning such subject matter.

8. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the "Relevant Companies") may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the "Relevant Information"). By entering into this Agreement, the Optionee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Optionee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Optionee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

9. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Optionee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

CRISPR THERAPEUTICS AG

By: ______________________________
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Optionee (including through an online acceptance process) is acceptable.

Dated: ______________________________

____
Optionee's Signature

Optionee's name and address:

____
____
____

Exhibit 10.20.4

RESTRICTED STOCK AWARD AGREEMENT
UNDER THE CRISPR THERAPEUTICS AG
2018 STOCK OPTION AND INCENTIVE PLAN

Name of Grantee: ______________________________

No. of Shares: ______________________

Grant Date: ______________________

Pursuant to the CRISPR Therapeutics AG 2018 Stock Option and Incentive Plan as amended through the date hereof (the "Plan"), CRISPR Therapeutics AG (the "Company") hereby grants a Restricted Stock Award (an "Award") to the Grantee named above. Upon acceptance of this Award, the Grantee shall receive the number of shares of Common Stock, par value CHF 0.03 per share (the "Stock") of the Company specified above, subject to the restrictions and conditions set forth herein and in the Plan. The Company acknowledges the receipt from the Grantee of consideration with respect to the par value of the Stock in the form of cash, past or future services rendered to the Company by the Grantee or such other form of consideration as is acceptable to the Administrator.

1. Award. The shares of Restricted Stock awarded hereunder shall be issued and held by the Company's transfer agent in book entry form, and the Grantee's name shall be entered as the stockholder of record on the books of the Company. Thereupon, the Grantee shall have all the rights of a stockholder with respect to such shares, including voting and dividend rights, subject, however, to the restrictions and conditions specified in Paragraph 2 below. The Grantee shall (i) sign and deliver to the Company a copy of this Award Agreement and (ii) deliver to the Company a stock power endorsed in blank.

2. Restrictions and Conditions.

(a) Any book entries for the shares of Restricted Stock granted herein shall bear an appropriate legend, as determined by the Administrator in its sole discretion, to the effect that such shares are subject to restrictions as set forth herein and in the Plan.

(b) Shares of Restricted Stock granted herein may not be sold, assigned, transferred, pledged or otherwise encumbered or disposed of by the Grantee prior to vesting.

(c) If the Grantee's employment with the Company and its Subsidiaries is voluntarily or involuntarily terminated for any reason (including death) prior to vesting of shares of Restricted Stock granted herein, all shares of Restricted Stock shall immediately and automatically be forfeited and returned to the Company.

3. Vesting of Restricted Stock. The restrictions and conditions in Paragraph 2 of this Agreement shall lapse on the Vesting Date or Dates specified in the following schedule so long as the Grantee remains an employee of the Company or a Subsidiary on such Dates. If a series of Vesting Dates is specified, then the restrictions and conditions in Paragraph 2 shall lapse only with respect to the number of shares of Restricted Stock specified as vested on such date.

Incremental Number of Shares Vested	Vesting Date
_____________ (___%)	____________
_____________ (___%)	____________
_____________ (___%)	____________
_____________ (___%)	____________
_____________ (___%)	____________

Subsequent to such Vesting Date or Dates, the shares of Stock on which all restrictions and conditions have lapsed shall no longer be deemed Restricted Stock. The Administrator may at any time accelerate the vesting schedule specified in this Paragraph 3.

4. Dividends. Dividends on shares of Restricted Stock shall be paid currently to the Grantee.

5. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Award shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

6. Transferability. This Agreement is personal to the Grantee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution.

7. Tax Withholding. The Grantee shall, not later than the date as of which the receipt of this Award becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event. Except in the case where an election is made pursuant to Paragraph 8 below, the Company shall have the authority to cause the required tax withholding obligation to be satisfied, in whole or in part, by withholding from shares of Stock to be issued or released by the transfer agent a number of shares of Stock with an aggregate Fair Market Value that would satisfy the withholding amount due.

8. Election Under Section 83(b). The Grantee and the Company hereby agree that the Grantee may, within 30 days following the Grant Date of this Award, file with the Internal Revenue Service and the Company an election under Section 83(b) of the Internal Revenue Code. In the event the Grantee makes such an election, he or she agrees to provide a copy of the election to the Company. The Grantee acknowledges that he or she is responsible for obtaining the advice of his or her tax advisors with regard to the Section 83(b) election and that he or she is relying solely on such advisors and not on any statements or representations of the Company or any of its agents with regard to such election.

9. No Obligation to Continue Employment. Neither the Company nor any Subsidiary is obligated by or as a result of the Plan or this Agreement to continue the Grantee in employment and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Subsidiary to terminate the employment of the Grantee at any time.

10. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Award and supersedes all prior agreements and discussions between the parties concerning such subject matter.

11. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the "Relevant Companies") may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the "Relevant Information"). By entering into this Agreement, the Grantee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Grantee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Grantee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

12. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Grantee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

CRISPR THERAPEUTICS AG

By: ______________________________
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Grantee (including through an online acceptance process) is acceptable.

Dated: ______________________________

____
Grantee's Signature

Grantee's name and address:

____
____
____

RESTRICTED STOCK UNIT AWARD AGREEMENT
FOR COMPANY EMPLOYEES
UNDER THE CRISPR THERAPEUTICS AG
2018 STOCK OPTION AND INCENTIVE PLAN

Name of Grantee: ____

No. of Restricted Stock Units: ______________________________

Grant Date: ______________________________

Pursuant to the CRISPR Therapeutics AG 2018 Stock Option and Incentive Plan as amended through the date hereof (the “Plan”), CRISPR Therapeutics AG (the “Company”) hereby grants an award of the number of Restricted Stock Units listed above (an “Award”) to the Grantee named above. Each Restricted Stock Unit shall relate to one share of Common Stock, par value CHF 0.03 per share (the “Stock”) of the Company.

1. Restrictions on Transfer of Award. This Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of by the Grantee, and any shares of Stock issuable with respect to the Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of until (i) the Restricted Stock Units have vested as provided in Paragraph 2 of this Agreement and (ii) shares of Stock have been issued to the Grantee in accordance with the terms of the Plan and this Agreement.

2. Vesting of Restricted Stock Units. The restrictions and conditions of Paragraph 1 of this Agreement shall lapse on the Vesting Date or Dates specified in the following schedule so long as the Grantee remains an employee of the Company or a Subsidiary on such Dates. If a series of Vesting Dates is specified, then the restrictions and conditions in Paragraph 1 shall lapse only with respect to the number of Restricted Stock Units specified as vested on such date.

Incremental Number of Restricted Stock Units Vested	Vesting Date
_____________ (___%)	_______________
_____________ (___%)	_______________
_____________ (___%)	_______________
_____________ (___%)	_______________

The Administrator may at any time accelerate the vesting schedule specified in this Paragraph 2.

3. Termination of Employment. If the Grantee's employment with the Company and its Subsidiaries terminates for any reason (including death or disability) prior to the satisfaction of the vesting conditions set forth in Paragraph 2 above, any Restricted Stock Units that have not vested as of such date shall automatically and without notice terminate and be forfeited, and neither the Grantee nor any of his or her successors, heirs, assigns, or personal representatives will thereafter have any further rights or interests in such unvested Restricted Stock Units.

4. Issuance of Shares of Stock. As soon as practicable following each Vesting Date (but in no event later than two and one-half months after the end of the year in which the Vesting Date occurs), the Company shall issue to the Grantee the number of shares of Stock equal to the aggregate number of Restricted Stock Units that have vested pursuant to Paragraph 2 of this Agreement on such date and the Grantee shall thereafter have all the rights of a stockholder of the Company with respect to such shares.

5. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Agreement shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

6. Tax Withholding. The Grantee shall, not later than the date as of which the receipt of this Award becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event. The Company shall have the authority to cause the required tax withholding obligation to be satisfied, in whole or in part, by withholding from shares of Stock to be issued to the Grantee a number of shares of Stock with an aggregate Fair Market Value that would satisfy the withholding amount due.

7. Section 409A of the Code. This Agreement shall be interpreted in such a manner that all provisions relating to the settlement of the Award are exempt from the requirements of Section 409A of the Code as "short-term deferrals" as described in Section 409A of the Code.

8. No Obligation to Continue Employment. Neither the Company nor any Subsidiary is obligated by or as a result of the Plan or this Agreement to continue the Grantee in employment and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Subsidiary to terminate the employment of the Grantee at any time.

9. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Award and supersedes all prior agreements and discussions between the parties concerning such subject matter.

10. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the "Relevant Companies") may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or

desirable for the administration of the Plan and/or this Agreement (the "Relevant Information"). By entering into this Agreement, the Grantee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Grantee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Grantee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

11. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Grantee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

CRISPR THERAPEUTICS AG

By: ______________________________
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Grantee (including through an online acceptance process) is acceptable.

Dated: ______________________________

____
Grantee's Signature

Grantee's name and address:
____
____
____

Exhibit 10.20.6

RESTRICTED STOCK UNIT AWARD AGREEMENT
FOR NON-EMPLOYEE DIRECTORS
UNDER THE CRISPR THERAPEUTICS AG
2018 STOCK OPTION AND INCENTIVE PLAN

Name of Grantee: ____

No. of Restricted Stock Units: ______________________________

Grant Date: ______________________________

Pursuant to the CRISPR Therapeutics AG 2018 Stock Option and Incentive Plan as amended through the date hereof (the "Plan"), CRISPR Therapeutics AG (the "Company") hereby grants an award of the number of Restricted Stock Units listed above (an "Award") to the Grantee named above. Each Restricted Stock Unit shall relate to one share of Common Stock, par value CHF 0.03 per share (the "Stock") of the Company.

1. Restrictions on Transfer of Award. This Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of by the Grantee, and any shares of Stock issuable with respect to the Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of until (i) the Restricted Stock Units have vested as provided in Paragraph 2 of this Agreement and (ii) shares of Stock have been issued to the Grantee in accordance with the terms of the Plan and this Agreement.

2. Vesting of Restricted Stock Units. The restrictions and conditions of Paragraph 1 of this Agreement shall lapse on the Vesting Date or Dates specified in the following schedule so long as the Grantee remains in service as a member of the Board on such Dates. If a series of Vesting Dates is specified, then the restrictions and conditions in Paragraph 1 shall lapse only with respect to the number of Restricted Stock Units specified as vested on such date.

Incremental Number of Restricted Stock Units Vested	Vesting Date
_____________ (___%)	_______________
_____________ (___%)	_______________
_____________ (___%)	_______________
_____________ (___%)	_______________

The Administrator may at any time accelerate the vesting schedule specified in this Paragraph 2.

3. Termination of Service. If the Grantee's service with the Company and its Subsidiaries terminates for any reason (including death or disability) prior to the satisfaction of the vesting conditions set forth in Paragraph 2 above, any Restricted Stock Units that have not vested as of such date shall automatically and without notice terminate and be forfeited, and

neither the Grantee nor any of his or her successors, heirs, assigns, or personal representatives will thereafter have any further rights or interests in such unvested Restricted Stock Units.

4. Issuance of Shares of Stock. As soon as practicable following each Vesting Date (but in no event later than two and one-half months after the end of the year in which the Vesting Date occurs), the Company shall issue to the Grantee the number of shares of Stock equal to the aggregate number of Restricted Stock Units that have vested pursuant to Paragraph 2 of this Agreement on such date and the Grantee shall thereafter have all the rights of a stockholder of the Company with respect to such shares.

5. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Agreement shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

6. Section 409A of the Code. This Agreement shall be interpreted in such a manner that all provisions relating to the settlement of the Award are exempt from the requirements of Section 409A of the Code as “short-term deferrals” as described in Section 409A of the Code.

7. No Obligation to Continue as a Director. Neither the Plan nor this Award confers upon the Grantee any rights with respect to continuance as a Director.

8. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Award and supersedes all prior agreements and discussions between the parties concerning such subject matter.

9. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the “Relevant Companies”) may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the “Relevant Information”). By entering into this Agreement, the Grantee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Grantee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Grantee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

10. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Grantee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

CRISPR THERAPEUTICS AG

By: ______________________________
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Grantee (including through an online acceptance process) is acceptable.

Dated: ______________________________

____
Grantee's Signature

Grantee's name and address:

____
____
____

CRISPR THERAPEUTICS AG

SENIOR EXECUTIVE CASH INCENTIVE BONUS PLAN

1. Purpose

This Senior Executive Cash Incentive Bonus Plan (the "***Incentive Plan***") is intended to provide an incentive for superior work and to motivate eligible executives of CRISPR Therapeutics AG (the "***Company***") and its subsidiaries toward even higher achievement and business results, to tie their goals and interests to those of the Company and its stockholders and to enable the Company to attract and retain highly qualified executives. The Incentive Plan is for the benefit of Covered Executives (as defined below).

2. Covered Executives

From time to time, the Compensation Committee of the Board of Directors of the Company (the "***Compensation Committee***") may select certain key executives (the "***Covered Executives***") to be eligible to receive bonuses hereunder. Participation in this Plan does not change the "at will" nature of a Covered Executive's employment with the Company.

3. Administration

The Compensation Committee shall have the sole discretion and authority to administer and interpret the Incentive Plan.

4. Bonus Determinations

(a) Corporate Performance Goals. A Covered Executive may receive a bonus payment under the Incentive Plan based upon the attainment of one or more performance objectives that are established by the Compensation Committee and relate to financial and operational metrics with respect to the Company or any of its subsidiaries (the "***Corporate Performance Goals***"), including, but not limited to, the following: research and development, publication, clinical and/or regulatory milestones cash flow (including, but not limited to, operating cash flow and free cash flow); revenue; corporate revenue; earnings before interest, taxes, depreciation and amortization; net income (loss) (either before or after interest, taxes, depreciation and/or amortization); changes in the market price of the Company's common stock; economic value-added; acquisitions or strategic transactions; operating income (loss); return on capital, assets, equity, or investment; stockholder returns; return on sales; gross or net profit levels; productivity; expense efficiency; margins; operating efficiency; customer satisfaction; working capital; earnings (loss) per share of the Company's common stock; bookings, new bookings or renewals; sales or market shares; number of customers, number of new customers or customer references; operating income and/or net annual recurring revenue, any of which may be (A) measured in absolute terms or compared to any incremental increase, (B) measured in terms of growth, (C) compared to another company or companies or to results of a peer group, (D) measured against the market as a whole and/or as compared to applicable market indices and/or (E) measured on a pre-tax or post-tax basis (if applicable). Further, any Corporate Performance Goals may be used to measure the performance of the Company as a whole or a business unit or other segment of the Company, or one or more product lines or specific markets. The Corporate Performance Goals may differ from Covered Executive to Covered Executive.

(b) Calculation of Corporate Performance Goals. At the beginning of each applicable performance period, the Compensation Committee will determine whether any significant element(s) will be included in or excluded from the calculation of any Corporate Performance Goal with respect to any Covered Executive. In all other respects, Corporate Performance Goals will be calculated in accordance with the Company's financial statements, generally accepted accounting principles, or under a methodology established by the Compensation Committee at the beginning of the performance period and which is consistently applied with respect to a Corporate Performance Goal in the relevant performance period.

(c) Target; Minimum; Maximum. Each Corporate Performance Goal shall have a "target" (100 percent attainment of the Corporate Performance Goal) and may also have a "minimum" hurdle and/or a "maximum" amount.

(d) Bonus Requirements; Individual Goals. Except as otherwise set forth in this Section 4(d): (i) any bonuses paid to Covered Executives under the Incentive Plan shall be based upon objectively determinable bonus formulas that tie such bonuses to one or more performance targets relating to the Corporate Performance Goals, (ii) bonus formulas for Covered Executives shall be adopted in each performance period by the Compensation Committee and communicated to each Covered Executive at the beginning of each performance period and (iii) no bonuses shall be paid to Covered Executives unless and until the Compensation Committee makes a determination with respect to the attainment of the performance targets relating to the Corporate Performance Goals. Notwithstanding the foregoing, the Compensation Committee may adjust bonuses payable under the Incentive Plan based on achievement of one or more individual performance objectives or pay bonuses (including, without limitation, discretionary bonuses) to Covered Executives under the Incentive Plan based on individual performance goals and/or upon such other terms and conditions as the Compensation Committee may in its discretion determine.

(e) Individual Target Bonuses. The Compensation Committee shall establish a target bonus opportunity for each Covered Executive for each performance period. For each Covered Executive, the Compensation Committee shall have the authority to apportion the target award so that a portion of the target award shall be tied to attainment of Corporate Performance Goals and a portion of the target award shall be tied to attainment of individual performance objectives.

(f) Employment Requirement. Subject to any additional terms contained in a written agreement between the Covered Executive and the Company, the payment of a bonus to a Covered Executive with respect to a performance period shall be conditioned upon the Covered Executive's employment by the Company on the bonus payment date. If a Covered Executive was not employed for an entire performance period, the Compensation Committee may pro rate the bonus based on the number of days employed during such period.

5. Timing of Payment

(a) With respect to Corporate Performance Goals established and measured on a basis more frequently than annually (e.g., quarterly or semi-annually), the Corporate Performance Goals will be measured at the end of each performance period after the Company's financial reports with respect to such period(s) have been published. If the Corporate Performance Goals and/or individual goals for such period are met, payments will be made as soon as practicable following the end of such period, but not later 74 days after the end of the fiscal year in which such performance period ends.

(b) With respect to Corporate Performance Goals established and measured on an annual or multi-year basis, Corporate Performance Goals will be measured as of the end of each such performance period (e.g., the end of each fiscal year) after the Company's financial reports with respect to such period(s) have been published. If the Corporate Performance Goals and/or individual goals for any such period are met, bonus payments will be made as soon as practicable, but not later than 74 days after the end of the relevant fiscal year.

(c) For the avoidance of doubt, bonuses earned at any time in a fiscal year must be paid no later than 74 days after the last day of such fiscal year.

6. Amendment and Termination

The Company reserves the right to amend or terminate the Incentive Plan at any time in its sole discretion.

Exhibit 21.1

Subsidiaries of the Registrant

Name of Subsidiary	Jurisdiction of Incorporation or Organization
CRISPR Therapeutics, Inc.	Delaware
CRISPR Therapeutics Ltd.	United Kingdom
TRACR Hematology Ltd	United Kingdom

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

(1) Registration Statement (Form S-3 No. 333-221491) of CRISPR Therapeutics AG,

(2) Registration Statement (Form S-8 No. 333-221427) pertaining to the CRISPR Therapeutics AG Amended and Restated 2016 Stock Option and Incentive Plan (the “Amended Plan”), and

(3) Registration Statement (Form S-8 No. 333-214184) pertaining to the CRISPR Therapeutics AG 2015 Stock Option and Grant Plan, the CRISPR Therapeutics AG 2016 Stock Option and Incentive Plan, the CRISPR Therapeutics AG 2016 Employee Stock Purchase Plan, the Non-Qualified Option Agreement with Megan Menner, the Non-Qualified Option Agreement with Paul Schneider, and the Non-Qualified Option Agreement with Pablo Cagnoni of CRISPR Therapeutics AG

of our report dated March 8, 2018, with respect to the consolidated financial statements of CRISPR Therapeutics AG included in this Annual Report (Form 10-K) of CRISPR Therapeutics AG for the year ended December 31, 2017.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 8, 2018

Exhibit 23.2

CONSENT OF INDEPENDENT AUDITORS

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

(1) Registration Statement (Form S-3 No. 333-221491) of CRISPR Therapeutics AG,

(2) Registration Statement (Form S-8 No. 333-221427) pertaining to the CRISPR Therapeutics AG Amended and Restated 2016 Stock Option and Incentive Plan (the “Amended Plan”), and

(3) Registration Statement (Form S-8 No. 333-214184) pertaining to the CRISPR Therapeutics AG 2015 Stock Option and Grant Plan, the CRISPR Therapeutics AG 2016 Stock Option and Incentive Plan, the CRISPR Therapeutics AG 2016 Employee Stock Purchase Plan, the Non-Qualified Option Agreement with Megan Menner, the Non-Qualified Option Agreement with Paul Schneider, and the Non-Qualified Option Agreement with Pablo Cagnoni of CRISPR Therapeutics AG

of our report dated March 8, 2018, with respect to the consolidated financial statements of Casebia Therapeutics LLP included in this Annual Report (Form 10-K) of CRISPR Therapeutics AG for the year ended December 31, 2017.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 8, 2018

Exhibit 31.1

CERTIFICATIONS

I, Samarth Kulkarni, certify that:

1. I have reviewed this Annual Report on Form 10-K of CRISPR Therapeutics AG;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 8, 2018

/s/ Samarth Kulkarni

Samarth Kulkarni
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Michael Tomsicek, certify that:

1. I have reviewed this Annual Report on Form 10-K of CRISPR Therapeutics AG;

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

   a) 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.

March 8, 2018

/s/ Michael Tomsicek

Michael Tomsicek
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of CRISPR Therapeutics AG (the "Company") for the year ended December 31, 2017, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned officers hereby certify, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350, that to the best of his or her knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 8, 2018	/s/ Samarth Kulkarni
	Samarth Kulkarni Chief Executive Officer (Principal Executive Officer)
Date: March 8, 2018	/s/ Michael Tomsicek
	Michael Tomsicek Chief Financial Officer (Principal Financial and Accounting Officer)